doi:10.1246/cl.2010.1206

Published on the web October 20, 2010

Acetylated Cyclodextrins as New Organogelators

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Acetylated cyclodextrins (CDs), including peracetylated α- and β-CDs as well as 2,3-*O*-diacetylated α- and β-CDs, were found to function as organogelators for organic solvents such as benzene, toluene, and xylenes at ambient temperature. Their organogelation capability was strongly affected by both the CD ring size and the degree of acetylation. Peracetylated α-CD showed the highest organogelation capability among these acetylated CDs, possibly due to the effective construction of three-dimensional networks by the pillar-like assemblies in the organic solvents.

Much attention has been paid to the construction of supramolecular architectures and materials using self-assembling approaches.[1] In particular, organogels formed by the self-assembly of low-molecular-weight organogelators in organic media have attracted considerable attention,[2,3] since they can be utilized as templates for materials synthesis[4] and as drug carriers.[5] The gelation of oils and organic solvents with such organogelators has been typically accomplished by the formation of three-dimensional networks from their one-dimensional fibrous self-assemblies, entrapping large amounts of oils and organic solvents. Thus far, a variety of low-molecular-weight organogelators have been prepared,[2,3] which include sugar-,[6] amino acid-,[7] and steroid-derived[8] compounds. In general, most of these organogelators have two characteristic segments: a lipophilic segment with affinity for oils and organic solvents, and an interactive segment (functional groups) to induce the formation of supramolecular assemblies.

Cyclodextrins (CDs) are cyclic oligosaccharides composed of several glucopyranose units and have multiple hydroxy groups on their upper and lower rims. The appropriate chemical modification of CDs is expected to produce novel organogelators bearing both a lipophilic segment and an interactive one, which can effectively generate three-dimensional networks through noncovalent forces such as hydrogen-bonding and van der Waals interactions. However, there have been only a few reports on cyclodextrin-derived organogelators.[9] The organogels formed with CD-derived gelators can potentially be used as molecular containers and drug carriers by utilizing the inclusion of guest molecules into the cavity of CD. Here, we report that acetylated CDs, including peracetylated α- and β-CDs as well as 2,3-*O*-diacetylated α- and β-CDs, form organogels in organic solvents through the construction of their unique supramolecular assembly. To the best of our knowledge, this is the first example of an organogelator composed of hydrophobically modified CDs.

Hexakis(2,3-*O*-diacetyl)-α-CD (DAc-α-CD), heptakis(2,3-*O*-diacetyl)-β-CD (DAc-β-CD), peracetylated α-CD (PAc-α-CD), and peracetylated β-CD (PAc-β-CD) (Figure 1) were easily prepared and characterized according to a previously reported method.[10] The gelation capability of these acetylated CDs toward various organic solvents was examined by the addition of increasing amounts of CD derivatives into oils and organic solvents at 20 °C with stirring. The gel formation was evaluated by visually observing the fluidity of mixtures of acetylated CDs with the organic solvents. Above the minimum gelation concentration, these mixtures showed no fluidity, and did not collapse over long periods of time after they had been turned upside down (Figure 2). These acetylated CDs successfully formed organogels in benzene, toluene, and xylenes. On the other hand, they showed no gelation capability toward non-aromatic hydrocarbon solvents such as hexane and cyclohexane. PAc-α- and -β-CDs showed gelation capability toward soybean oil (the minimum gelation concentrations of PAc-α- and -β-CDs in soybean oil were 180 and 600 g L^{-1}, respectively), in contrast to DAc-α- and -β-CDs that formed no gels in soybean oil. These soybean oil gels were stable even when they were heated up to 80 °C. Figure 3 shows the minimum concentration of acetylated CDs required to induce gelation of the aromatic solvents at 20 °C. The gelation capability of acetylated CDs was barely influenced by the types of aromatic solvents used, except for DAc-α-CD whose gelation capability toward benzene and toluene was higher than toward xylenes. In the cases of both DAc- and PAc-CDs, the α-CD derivative showed higher gelation capability toward most of the aromatic solvents as compared to the β-CD derivative, indicating that the organogelation capability of acetylated CDs is strongly affected by the ring size of the CD backbone. Interestingly, PAc-CDs tended to

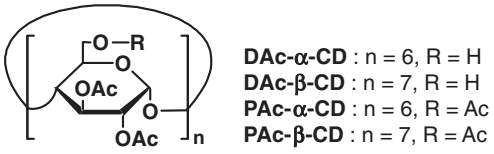

Figure 1. Chemical structures of acetylated cyclodextrins.

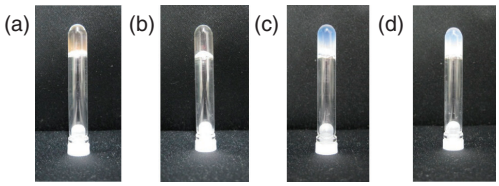

Figure 2. Photographs of benzene gels formed with various acetylated cyclodextrins: (a) DAc-α-CD, (b) DAc-β-CD, (c) PAc-α-CD, and (d) PAc-β-CD.

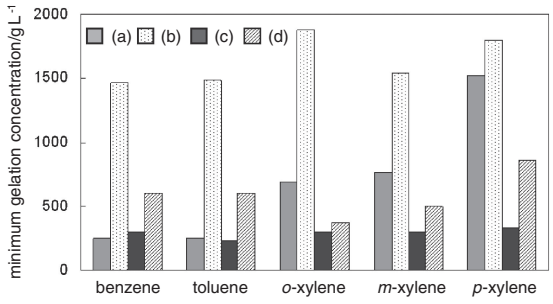

Figure 3. Minimum gelation concentration of acetylated cyclodextrins in various aromatic solvents: (a) DAc-α-CD, (b) DAc-β-CD, (c) PAc-α-CD, and (d) PAc-β-CD.

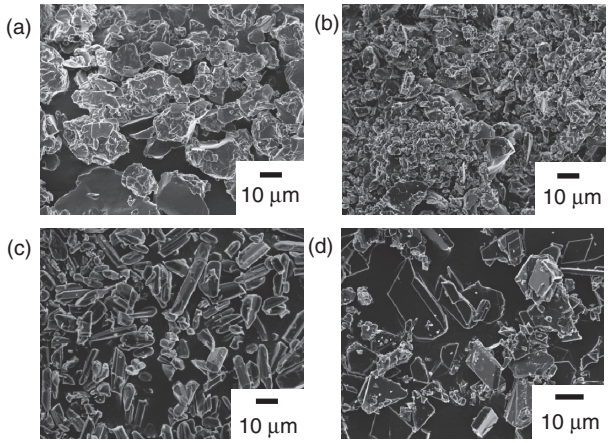

Figure 4. SEM images of xerogels from benzene gels formed with acetylated CDs: (a) DAc-α-CD, (b) DAc-β-CD, (c) PAc-α-CD, and (d) PAc-β-CD.

form organogels more effectively than DAc-CDs, despite the fact that the former does not have any free hydroxy groups which are considered to be important for three-dimensional network formation in an organic solvent. In particular, PAc-β-CD showed higher gelation capability toward all of the aromatic solvents examined here as compared to DAc-β-CD. These findings suggest that morphology and/or properties of supramolecular assemblies formed with PAc-α- and -β-CDs in organic solvents may be considerably different from those formed with DAc-α- and -β-CDs.

In order to understand the mechanism responsible for organogel formation with these acetylated CDs, SEM observation of the corresponding xerogels (dried gels) was performed. Figure 4 shows SEM images of the xerogels from benzene gels formed with acetylated CDs. Interestingly, the xerogels formed with PAc-α- and -β-CDs comprised pillar-like and plate-like microstructures, respectively, in contrast to the xerogels formed with DAc-α- and -β-CDs, where only non-regular clusters were observed. In the xerogels from toluene and *o*- and *m*-xylene gels formed with PAc-α-CD, formation of micropillars was clearly observed (Figure 5). Although there have been many reports on organogel formation through the fibrous assembly of saccharide derivatives,[3b,6] organogels formed through the assembly of micropillars composed of saccharide derivatives are rare. These results suggest that microstructures formed with acetylated CDs

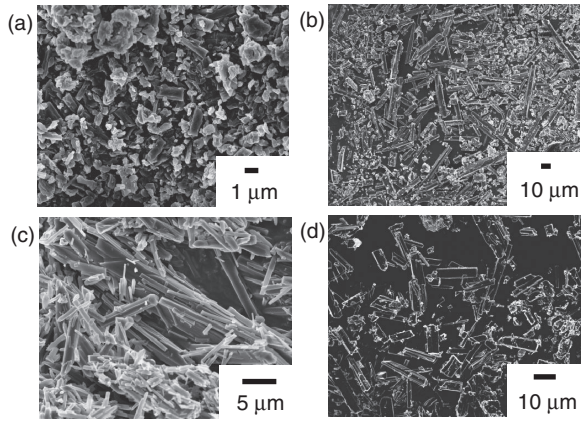

Figure 5. SEM images of xerogels from various organogels formed with PAc-α-CD: (a) toluene gel, (b) *o*-xylene gel, (c) *m*-xylene gel, and (d) *p*-xylene gel.

largely affect organogel formation, possibly through the formation of three-dimensional networks by noncovalent forces such as London dispersion forces and van der Waals interactions. The relatively high gelation capability of PAc-α-CD indicates that the pillar shapes of these microstructures contribute to the effective construction of three-dimensional networks in the organic solvents. Although the gelation capability of these acetylated CDs toward organic solvents is lower than that of conventional organogelators,[2,3] precise control of the size and shape of the microstructures formed with acetylated CDs in organic solvents would improve their gelation capability further.

The rheological properties of these organogels were also examined. In the plots of the storage modulus G' and the loss modulus G'' of a soybean oil gel formed with PAc-α- or -β-CD against angular frequency, the G' value was higher than the G'' value over a range of angular frequencies from 0.1 to 10 rad s^{-1} (see Figures S9 and S10 in the Supporting Information).[11] This indicates that PAc-α- and -β-CDs clearly form gels in soybean oil.

In conclusion, we have demonstrated that acetylated CDs show gelation capability toward organic solvents such as benzene, toluene, and xylenes. In particular, peracetylated α-CD bearing no free hydroxy groups exhibited the highest gelation capability among the acetylated CDs examined here. This organogel formation is presumed to be due to the formation of a three-dimensional network of microstructures composed of acetylated CD assemblies, trapping the solvents within the voids of the network. These organogels can be potentially used as molecular containers and drug carriers by utilizing the inclusion of specific molecules into the CD cavity.

References and Notes

1 a) L. M. Bronstein, in *Encyclopedia of Nanoscience and Nanotechnology*, ed. by H. S. Nalwa, American Scientific Publishers, **2004**, Vol. 7, p. 193. b) J. Li, X. J. Loh, *Adv. Drug Delivery Rev.* **2008**, *60*, 1000. c) J. W. Goodby, I. M. Saez, S. J. Cowling, V. Görtz, M. Draper, A. W. Hall, S. Sia, G. Cosquer, S.-E. Lee, E. P. Raynes, *Angew. Chem., Int. Ed.* **2008**, *47*, 2754. d) H.-J. Kim, Y.-B. Lim, M. Lee, *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 1925. e) Y. Wan, Y. Shi, D. Zhao, *Chem. Mater.* **2008**, *20*, 932.

2 P. Terech, R. G. Weiss, *Chem. Rev.* **1997**, *97*, 3133.
3 a) J. H. van Esch, B. L. Feringa, *Angew. Chem., Int. Ed.* **2000**, *39*, 2263. b) O. Gronwald, E. Snip, S. Shinkai, *Curr. Opin. Colloid Interface Sci.* **2002**, *7*, 148. c) N. M. Sangeetha, U. Maitra, *Chem. Soc. Rev.* **2005**, *34*, 821.
4 M. Llusar, C. Sanchez, *Chem. Mater.* **2008**, *20*, 782.
5 A. Vintiloiu, J.-C. Leroux, *J. Controlled Release* **2008**, *125*, 179.
6 a) K. Yoza, Y. Ono, K. Yoshihara, T. Akao, H. Shinmori, M. Takeuchi, S. Shinkai, D. N. Reinhoudt, *Chem. Commun.* **1998**, 907. b) G. John, G. Zhu, J. Li, J. S. Dordick, *Angew. Chem., Int. Ed.* **2006**, *45*, 4772.
7 a) K. Hanabusa, K. Okui, K. Karaki, T. Koyama, H. Shirai, *J. Chem. Soc., Chem. Commun.* **1992**, 1371. b) K. Hanabusa, R. Tanaka, M. Suzuki, M. Kimura, H. Shirai, *Adv. Mater.* **1997**, *9*, 1095.
8 M. George, R. G. Weiss, *Acc. Chem. Res.* **2006**, *39*, 489.
9 a) C. de Rango, P. Charpin, J. Navaza, N. Keller, I. Nicolis, F. Villain, A. W. Coleman, *J. Am. Chem. Soc.* **1992**, *114*, 5475. b) T. Kida, Y. Marui, K. Miyawaki, E. Kato, M. Akashi, *Chem. Commun.* **2009**, 3889. c) Y. Marui, T. Kida, M. Akashi, *Chem. Mater.* **2010**, *22*, 282. d) W. Deng, D. H. Thompson, *Soft Matter* **2010**, *6*, 1884. e) Y. Marui, A. Kikuzawa, T. Kida, M. Akashi, *Langmuir* **2010**, *26*, 11441.
10 K. Takeo, H. Mitoh, K. Uemura, *Carbohydr. Res.* **1989**, *187*, 203.
11 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

