From Supramolecular Hydrogel to Macroscopic Spheres: Nucleation-controlled Polymorphic Transition

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A new kind of hydrogelator based on a *p*-hydroxypyridinium salt of 1,2,4-benzenetricarboxylic acid formed standard hydrogel at higher concentration, while self-assembled to globular structures at lower concentration, which could be explained by nucleation-controlled processes.

In recent years many systematic studies have demonstrated how molecules assemble spontaneously into structures with high complexity and dimensionality. A fascinating aspect of the emerging field is to explore strategies for producing different morphologies with structural definition from nano-to macroscopic scale. Supramolecular hydrogels derived from building blocks of low molecular weight gelators have gained considerable attention recently owing to their responsive performances and many potential applications.[1,2] These gels generally consist of three-dimensional networks in which self-assembled one-dimensional fibers are capable of immobilizing water as a consequence of capillary forces and surface tension. Some researchers have tried to investigate different morphologies that can underpin gel-phase materials (lamellar, vesicle, and platelet) and control the morphologies based on component structures,[3,4] solvent properties,[5,6] or the ratio of different components.[7,8] Despite of these studies, there is little predictive understanding of the formation of these morphologies, and little work has been devoted to the aggregates that they might form at concentration (c) below the minimum gelation concentration (MGC). In this paper, we found that a new kind of hydrogelator (defined as G, see Figure 1a) based on *p*-hydroxypyridinium salt of 1,2,4-benzenetricarboxylic acid formed standard hydrogel at $c \geq$ MGC, but self-assembled to micrometer-sized spheres at $c <$ MGC.

The gelator (G) was prepared from 1,2,4-benzenetricarboxylic acid (TCA) and 4-hydroxypyridine (PHP) in 80% yield by our previous procedure[9] with the details shown in the Supporting Information.[10] Based on the structures of some similar gelators,[9,11,12] we proposed a possible structure for G illustrated in Figure 1a, in which two PHP units are hydrogen bonded to the two *o*-carboxylic groups of TCA. G is able to gel water efficiently with a MGC of 40 mg·mL^{-1}. The linear viscoelastic frequency sweep response of the gel exhibits weak frequency dependence from 0.1 to 100 Hz (with the moduli at around 10^5 Pa in Figure 1b), demonstrating an ordinary, highly elastic gel.[13] In addition, scanning electron microscopy (SEM) (Figure 1c) of the xerogel indicates formation of entangled fibrillar networks. The gel formed at gelator concentration of 5 wt % has a gel-to-sol dissociation temperature (T_{gel}) of 65 °C.

Interestingly, an aqueous solution of G at $c <$ MGC generated regular spheres rather than gel after several days' storage without any stimulus from the environment. The suspension of G (0.05 g in 2 mL of water) was heated to a transparent solution. After standing the solution at 20 °C for more than 5 h, spheres appeared and grew larger as time passed by until minimeter-sized spheres were formed. The spheres can be dissolved and self-assemble many times through the heating–cooling process. Although G has similar chemical structure as some other gelators derived from 1,2,4,5-benzenetetracarboxylic acid and hydroxypyridines,[11,12] this regular assembled structure is rather peculiar. The lack of one carboxylic group and the unsymmetrical structure of G play a major role in the process. After dehydration under vacuum environment, the spheres display porous microstructure as analyzed by SEM. From the cross section, a standard fibrillar structure is clearly observed (as shown in Figure 2).

We destroyed the spheres by using an ultrasonator and investigated the resulting suspension by transmission electron microscopy (TEM). Similar to the SEM images, rod-like fibers are observed with the width of 100 nm.[10] To see the details of the self-assembling process, the gelator solution was observed directly with an OLYMPUS BH-2 phase contract microscope (PCM) with a CCD at room temperature. The results in Figure 3 indicate that after formation of the initial crystals, the molecules assembled spontaneously onto crystals from all directions until macroscopic spheres were obtained eventually.

Because of the branching structure, single crystals of G are difficult to obtain. But we tried to get a single crystal of TCA, whose structure indicates that two TCA molecules connect with each other via the double hydrogen bonds between the two

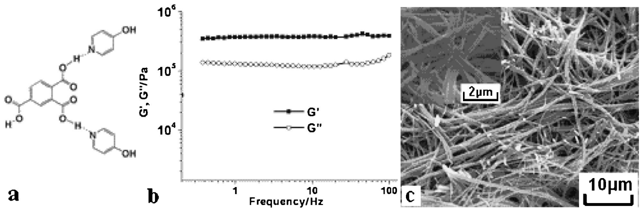

Figure 1. (a) Structure of G; (b) dynamic moduli, G′ (solid) and G″ (hollow) vs. frequency for the gel formed at 5 wt % of G; (c) SEM image of the xerogel formed at 5 wt % of G.

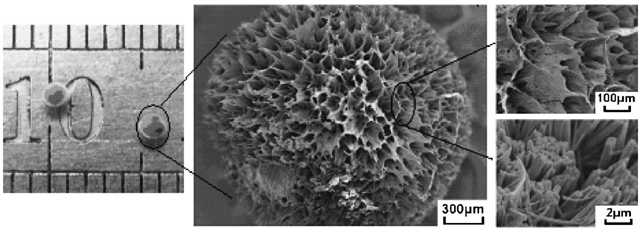

Figure 2. Self-assembled macroscopic spheres at 2.5 wt % of G.

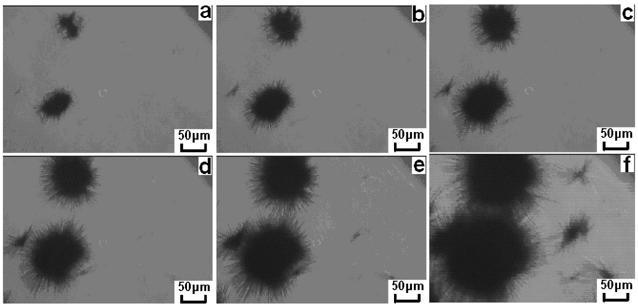

Figure 3. PCM images of solution samples of G in situ observation (formed at 2.5 wt % G) during storage. The time interval between two neighboring photographs is 2 h.

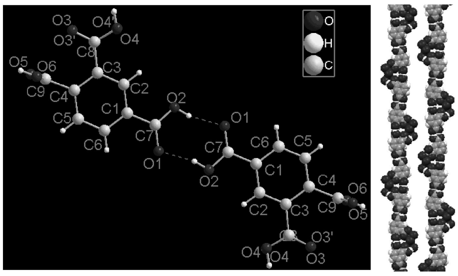

Figure 4. Molecular structure of TCA with atom labeling (left) and side view of the assembled chains of space-filling mode (right).

carboxylic groups at the 4-position (Figure 4). According to a crystal of a model complex formed from *o*-phthalic acid and PHP,[9] both of the carboxylic groups in *o*-phthalic acid can form hydrogen bonds with the pyridine group of PHP. Meanwhile, the phenolic hydroxy group of PHP becomes electron deficient and serves as a proton donor to form hydrogen bonds with other groups. In both crystals, the molecules are able to connect together into one-dimensional structures. These results are helpful to understand the molecular structure of G (Figure 1a) and provide information for the assembling fashion of the molecules. The self-assembling processes under different gelator concentrations are illustrated in Figure 5. Due to the asymmetric structure of G, the initial branching crystal nucleus makes the fibers grow from different directions,[14] and crystallographic mismatch branching occurs during the fiber-growing process in both cases even though the assembling backbone is mainly fiber-like.

At $c <$ MGC (low supersaturation), the nucleation barrier is very high, hence the number of nuclei should be rather small. The growth of crystals is actually a process of delivering assembling units from the solution to the crystal surface. The crystallographic mismatch accelerates the process, enlarges the size of the structures, and finally leads to sphere-like aggregates. We also found some twin spheres in the solution combining by two separate spheres together, which is another evidence supporting the nucleation-fiber formation-mismatch growth process.

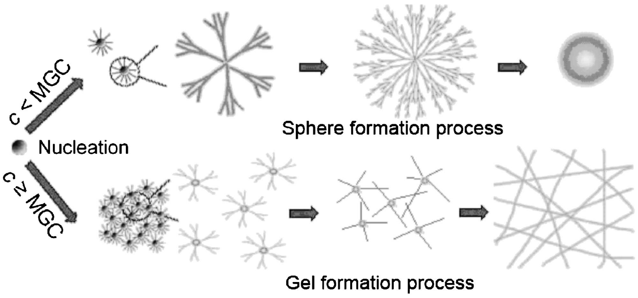

Figure 5. Schematic representation of the self-assembling processes.

However, at $c \geq$ MGC (high supersaturation), the growth of fibers becomes kinetically favored, the number of nucleation centers increases, and the irregular mismatch gives rise to the formation of fibrillar networks and finally the gel. These nucleation-controlled processes could explain why different morphologies are obtained by varying the gelator concentration.

In summary, we reported the self-assembling of gelator molecules into macroscopic spheres and supramolecular hydrogel. The current method has the advantage of generating self-assemblies of different size and shape simply by adjusting the gelator concentration. This investigation may provide some insights into the early stages of the aggregation of gelators before fibers growth and trappment of solvent, which is helpful for understanding the gelation mechanism.

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