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pH-responsive Dendritic Gelators

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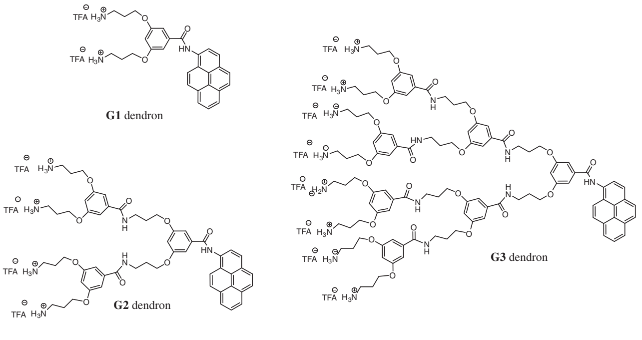
The pH responsibility of cationic charged dendrons, which were previously synthesized for DNA-sensing applications, was investigated. The first and second generation amide dendrons **G1** and **G2** formed hydrogels under basic conditions, but the hydrogel returned to the fluid state under acidic conditions; this process was completely reversible. In addition, the fluorescence of the diluted **G1**, **G2**, and **G3** solutions also showed a high sensitivity to the pH value.

Dendrimers are characterized by their hierarchical three-dimensional structures consisting of a multifunctional core from which successive branched repeating units radiate outward.[1–4]

Dendritic gelators, which would bridge the gap between polymeric and small molecular gelators, have gained increasing attention due to their well-defined and readily controlled structures. Since Newkome et al. reported the first example of a dendritic gelator in 1986,[5] several research groups have independently reported different kinds of dendritic gelators.[6–14] In addition, most of them are thermoreversible and photoreversible dendritic gelators,[11,13] and gelators which response to fluoride ions[15] have been recently reported. However, there are few reports about pH-responsive dendritic gelators.

We recently synthesized a series of water-soluble cationic pyrene-dendron derivatives **G1**, **G2**, and **G3** (Scheme 1) and measured its DNA detection ability.[16] During this investigation, we found that the dendrons form pH-responsive hydrogels. We now report the detailed properties of such pH-responsible dendritic gelators.

Supramolecular gels generated through the self-assembly of small gelator molecules via physical interactions like hydrogen bonding, π–π stacking, hydrophobic interactions, donor–acceptor interactions, or van der Waals interactions form entangled fibril networks.[17–19] Based on these characteristics of the gel formations, we expected that the π–π interactions between the pyrene moieties and hydrogen bonding between the amine and amide groups under basic conditions both provide a sufficient force required for the generation of extended fibril nanostructures. After the addition of a stoichiometric ratio of an aqueous NaOH solution, **G1** and **G2** show excellent abilities to form gels at the gelator concentration of ca. 14×10^{-3} and 3.5×10^{-3} M, respectively. However, **G3** failed to form gels under similar conditions probably due to its relatively large size, which caused an increase of the steric hindrance and reduction of its flexibility between intermolecular interactions to form hydrogels.



Scheme 1. Chemical structures of **G1**, **G2**, and **G3** dendrons.

Figure 1 shows the optical images of the supramolecular gels of **G1** and **G2** with the addition of a stoichiometric amount of base. The hydrogel of **G1** appeared opaque, indicating the presence of insoluble microparticles in the hydrogel. This might be due to the limited solubility of **G1**. On the contrary, the hydrogel of **G2** was transparent. **G1** and **G2** showed the ability to form gels at the pH values of 12.4 and 11.5, respectively. The gels changed back immediately to fluid solutions at around pH 7.0 after adding HCl to adjust the pH value by protonating the basic sites of gelators. This sol–gel phase transition can be reversibly switched without affecting the gelation ability. An SEM analysis was also performed to study the morphologies of the hydrogels of **G1** and **G2** (Figure 2).

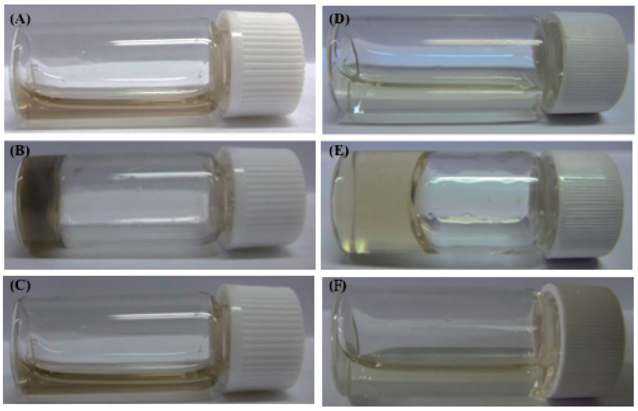


Figure 1. Optical images of supramolecular gels of **G1** and **G2** before [(A) and (D)] and after adding stoichiometric amount of aqueous NaOH [(B) and (E)] or HCl [(C) and (F)] solution.

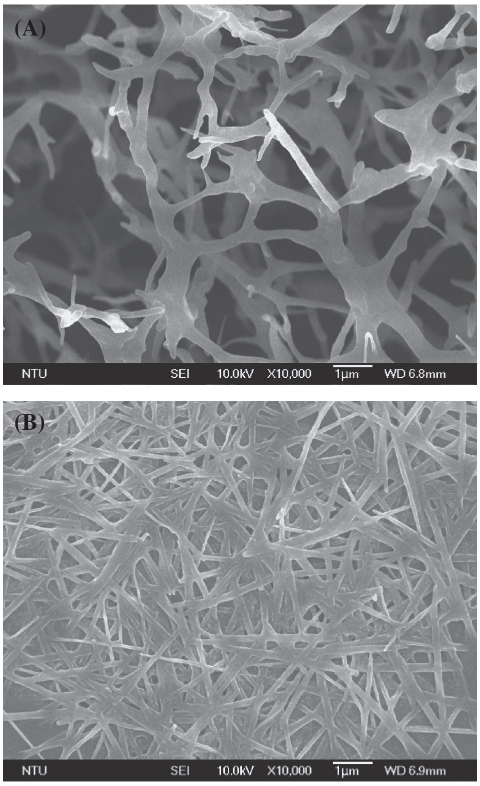


Figure 2. SEM images of hydrogels (A) **G1** and (B) **G2**.

G1 exhibits an entangled irregular fibrous matrix with widths around 200 to 500 nm. This irregular morphology might suggest that there should be more than one type of aggregation process for the hydrogel network. The morphology of **G2** shows fine nanofibers with widths from 100 to 300 nm, which significantly differs from that of the fibrous matrix formed by **G1**. These well-developed fibrous networks indicate that supramolecular interactions (hydrogen bonding and π–π stacking) promote the self-assembly of the small molecular gelator to form long and polymer-like fibrous networks that mainly trap the water by surface tension.

In addition, the fluorescent responses of the **G1**–**G3** to various NaOH concentrations under dilute conditions (0.5×10^{-4} M) were investigated and shown in Figure 3A and Figure S1 in Supporting Information.[20]

During titration with an aqueous NaOH solution, the **G1**–**G3** solutions showed a broad emission band of pyrene at 375 to 610 nm with an excitation at 340 nm and gradual increase in their fluorescence intensities. With the addition of NaOH at the equivalent concentration ($[OH]/[NH_3^+] = 1$), **G3** was completely deionized and showed a large fluorescence enhancement and saturation, which suggests that the pyrene moiety is reorganized to form excimers (Figure S1B[20]). The increase in fluorescence might be due to the strong tendency of the pyrene group to form dimers or oligomers in an aqueous solution after deionization of the dendrons, which eliminated the cationic repulsion and increased the molecular interaction (e.g., hydrogen bonding, etc.). On the other hand, **G1** and **G2** showed large fluorescence enhancements and reached a fluorescence saturation at $[OH]/[NH_3^+] = 0.75$, indicating that **G1** and **G2** more favorably form pyrene excimers in the aqueous phase, despite the existence of a partial cationic repulsion. This might be because **G1** and **G2** have less steric hindrance compared to that of **G3**.

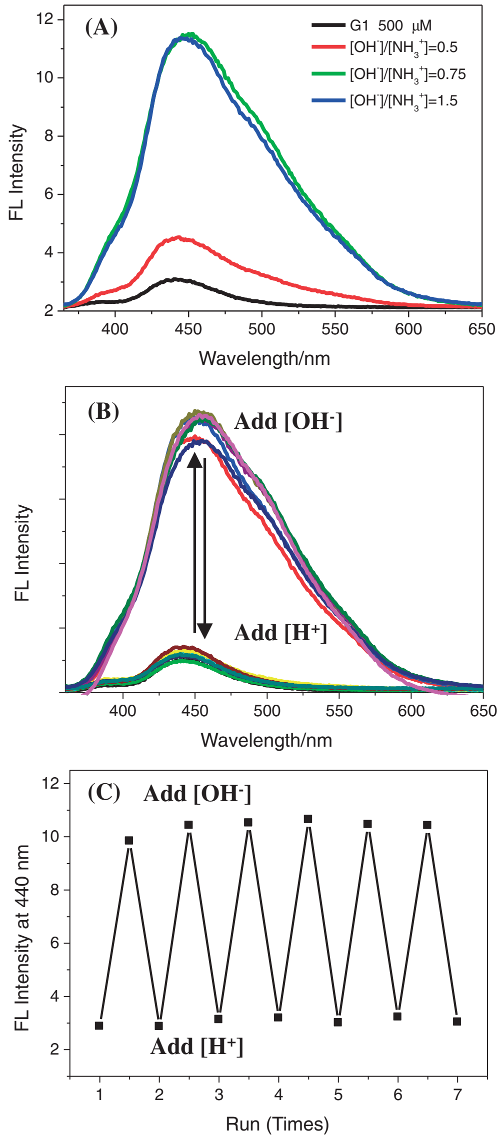


Figure 3. (A) Fluorescence emission of **G1** at concentration of 5×10^{-4} M and at various NaOH concentrations. Excitation wavelength is at 340 nm. (B) Fluorescence emission of **G1** with repeating addition of equivalent concentration of aqueous NaOH or HCl solution. (C) Reversible response of **G1** by the addition of aqueous NaOH or HCl solution illustrated with its fluorescence intensity at 440 nm.

Thus, the excimer formations of **G1** and **G2** are more pronounced with less added NaOH. These results are in agreement with the results of the pH-responsive hydrogel fabrication. The addition of an equivalent amount of acid (HCl aqueous solution) to the deionized dendron solution, which was slightly cloudy, turned it into a clear solution. Moreover, the addition of an equivalent amount of acid caused a decrease in their fluorescence intensities, indicating the disappearance of the excimer band of pyrene (as shown in Figure 3B). Their pH responses of the **G1**–**G3** solution are completely reversible as shown in Figures 3C and S2.[20]

In summary, we have described the pH-responsive dendritic gelators **G1** and **G2** which showed reversibility and entangled fibrous structures at appropriate pH values. However, **G3** did not form hydrogel due to its higher steric hindrance. It was also found that all generation dendrons **G1**, **G2**, and **G3** showed reversible pH-responsive fluorescent properties.

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20 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.