Low-Molecular-Weight Hydrogelators Based on L-Lysine with Various Pyridinium Cations

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L-Lysine derivatives act as low-molecular-weight hydro-gelators that can gel water below 1 wt%.

Organogels of low-molecular-weight compounds (organo-gelators) are one of the new fields of supramolecular chemistry and a novel class of materials.[1] Often these materials are characterized by the formation of hierarchical structures, i.e., by organization on more than one length scale through noncovalent interactions (hydrogen bonding, π-π stacking, charge transfer, and van der Waals interactions). Many organogelators that form a hierarchical network of superstructures in organic fluids have now been synthesized.[2–5] Furthermore, the formation of hydro-gels using low-molecular-weight compounds, referred to as hydrogelators, has also been focused.[6]

One of our challenges is the development of hydrogelators based on organogelators. Hydrogelators should be water-soluble, but most organogelators are insoluble or very low soluble in water because they usually include long alkyl chains and other hydrophobic segments. We focused on the L-lysine derivatives, which are one of the best organogelators.[7] In order to make them water-soluble, positively charged segments were attached and compounds 1–6 were synthesized. These were readily dissolved in water with mild heating (ca. 40 °C) and then, after allowing the solution to stand at room temperature, hydrogels were formed. Here we describe a family of low-molecular-weight hydrogela-tors and their gelation behavior in water.
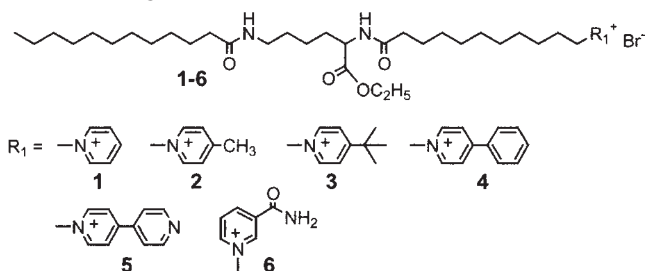
Compounds 1–6 were prepared from commercially available N^{ε}-lauroyl-L-lysine (Ajinomoto Co., Ltd.) according to a synthetically simple approach-esterification, acylation, and quaternization. The gelation ability of these compounds was evaluated by a test tube upside-down method after allowing the hot solutions to stand at room temperature for 6 h.

The gelation test and the values of the minimum gel concentration (MGC) necessary for the gelation of water are listed in Table 1. 1–5 can gel water below 1 wt%; particularly, both 3 and 4 form hydrogels at 0.2 wt%, which corresponds to the fact that a gelator molecule entraps more than 20,000 water molecules. In contrast, 6 was readily soluble in water with mild heating (ca. 40 °C) and failed to gel water. However, it should be mentioned that 6 formed the transparent highly-viscous solution

Table 1. Results of gelation test for 1–6 in water

|	State	MGC[a]
1	Gel (Transparent)	3
2	Gel (Transparent)	5
3	Gel (Translucent)	2
4	Gel (Opaque)	2
5	Gel (Opaque)	10
6[b]	VS (≤0.2 wt%)	
	P (>0.2 wt%)	

[a]Minimum gel concentration necessary for hydrogel forma-tion (mg/ml).
[b]The aqueous solution of 6 was a transparent and highly viscous solution below 0.2 wt%, while 6 precipitated above 0.2 wt%. VS: highly viscous solution. P: Precipitation.

at 0.2 wt% (2 mg/ml), it precipitated above 0.2 wt% though. It is likely that 6 readily crystallizes above 0.2 wt% because it has more hydrogen bonding sites on the pyridinium ring than other compounds.

Figure 1 shows TEM images of the samples prepared from 1, 3, 4, and 6 in dilute aqueous solution.[8] 1, 3, and 4 self-assembled into the nanoscale fibrous structure with 15–20 nm for 1, 40–100 nm for 3, and 40–300 nm for 4 and created three-dimensional (3D) network structures by entanglement of the self-assembled nanofibers. This fact implies that the hydrogels are formed by entrapping water molecules into the spaces of the 3D networks. Very interestingly, the aspect of the gels depends on the thickness of the self-assembled nanofibers; the hydrogels made by the narrow fibers (1) and the wide ones (4) show a transparency and opacity, respectively, and 3 with the intermediate thickness produces the translucent hydrogel. On the other hand, 6 also forms self-assembled nanofibers in the dilute aqueous solution, which leads to a highly viscous solution. The further addition of 6 more than 0.2 wt% caused crystallization due to the strong hydrogen bonding interaction induced by the amide group on the pyridinium ring, but not gelation.
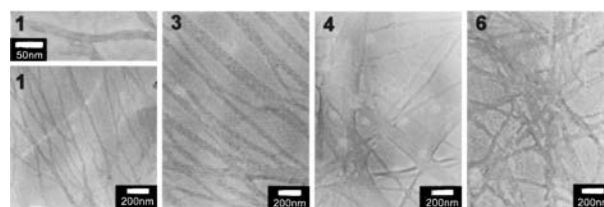
Figure 1. TEM images of samples prepared from 0.1 wt% aqueous solutions of 1, 3, 4, and 6.

To elucidate the gelation mechanism, the FTIR spectra and fluorescence spectra using 8-anilino-1-naphthalenesulfonic acid

(ANS) as a probe were measured. Figure 2 shows the FTIR spectra of the hydrogels formed by **2** in D_2O[9] and the isotropic solution of **2** in $CHCl_3$. The FTIR spectrum of **2** in chloroform solution shows absorption bands at $1660\,cm^{-1}$ and $1514\,cm^{-1}$, characteristic of non-hydrogen bonded C=O (amide I) and N–H (amide II), respectively. In the FTIR spectrum of **2** in D_2O gel, the absorption bands of the C=O stretching vibration (νC=O, amide I) and N–H bending vibration (δN–H, amide II) shift to $1635\,cm^{-1}$ and $1546\,cm^{-1}$, which are assigned to the hydrogen bonded amide groups. Furthermore, we can also obtain information on the alkyl groups from the FTIR spectra. The absorption bands of the asymmetric (ν_{as}) and symmetric (ν_s) CH_2 stretching vibrational modes of **2** were observed at $2928\,cm^{-1}$ (ν_{as}, C–H) and $2858\,cm^{-1}$ (ν_s, C–H) in $CHCl_3$, while they shift to $2920\,cm^{-1}$ and $2850\,cm^{-1}$ in D_2O. Such a lower wavenumber shift indicates a decrease in the fluidity of the alkyl chains in **2**,[10] which is induced by the strong organization of the alkyl groups in the self-assembled nanofibers presumably via a hydrophobic interaction.
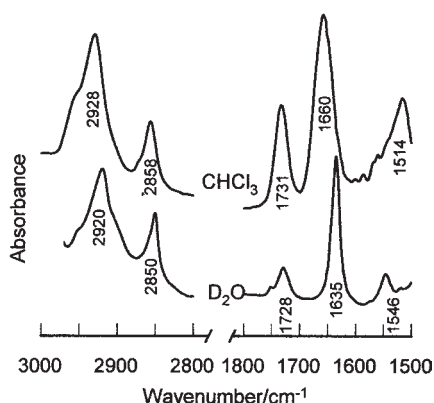
Figure 2. FTIR spectra of hydrogel formed by **2** in D_2O and isotropic solution of **2** in $CHCl_3$.

Figure 3 shows the fluorescence spectra of ANS in aqueous solutions containing various concentrations of **2**. By the addition of **2** (1 mM), the fluorescence maxima (λ_{max}) blue-shifts from 534 nm to 474 nm, and the further addition increases the
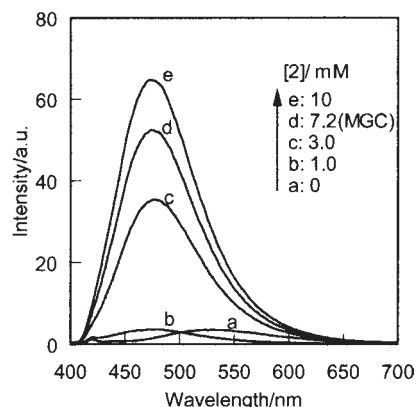
Figure 3. Fluorescence spectra of ANS in aqueous solutions containing various concentrations of **2**. [ANS] = 1.0×10^{-5} M.

fluorescence intensity and produces almost constant λ_{max} values. Such fluorescence behavior indicates that the ANS molecules are incorporated into the hydrophobic environment in the self-assembled nanofibers. One of the driving forces for the self-assembly of **2** into nanofibers is hydrophobic interaction, which is supported by the FTIR result in D_2O.

In summary, we developed low-molecular-weight hydro-gelators based on L-lysine derivatives that can be simply and effectively synthesized. In water, these compounds first self-assemble into nanofibers through hydrogen bonding and hydrophobic interactions, and then grow into 3D network structures by entanglement of the nanofibers, leading to the formation of hydrogels.

References and Notes
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8   Samples were prepared from an aqueous solution of the 0.1 wt% gelator.
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