

## Novel family of low molecular weight hydrogelators based on L-lysine derivatives

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**New L-lysine derivatives with a positively charged terminal can gel water below 1 wt%; particularly, 1a and 2a form a hydrogel at 0.3 wt% corresponding to approximately 12,300 and 12,500 waters/gelator molecule, respectively.**

Organogelators of low molecular weight compounds, which are capable of immobilizing organic solvents, are one of the new fields of supramolecular chemistry and a novel class of materials.<sup>1</sup> Many organogelators have been reported in the literature.<sup>2</sup> These organogelators can organize many monomeric species into complex higher-order structures such as fibrous, tubular, and helical structures in organic solvents through hydrogen bonding (amide, urea, hydroxy, etc.) and van der Waals interaction (long alkyl, aromatic groups, etc.).

The hydrogels based on synthetic polymers and biopolymers are widely employed in various material applications such as a transport medium for dissolved species as a link between body fluids and synthetic implants.<sup>3</sup> However, examples are indeed rare for nonpolymeric hydrogel formers.<sup>4</sup> Most of the organogelators are rarely used as a hydrogelators due to their poor solubility or insolubility as well as high crystallinity in water. For application of the organogelators as hydrogelators, we first tried introducing a positive charge into an organogelator. Interestingly, we found that compound **2a** was readily dissolved in water with heating which led to the formation of a gel. Here we describe new hydrogelators based on L-lysine derivatives with various positively charged terminals. In addition, we discuss the effect of alkyl length in the ester group and of the alkylene spacer length between the positively charged terminal and L-lysine segment on gelation behavior.

All the L-lysine derivatives were prepared from commercially available *N*<sup>ε</sup>-lauroyl-L-lysine from Ajinomoto Co., Ltd., according to a synthetically simple approach—esterification, acylation with *n*-bromoalkanoyl chloride, and then quaternization. The gelation ability of these compounds was evaluated by the 'stable to inversion of a test tube' method.<sup>4d†</sup>

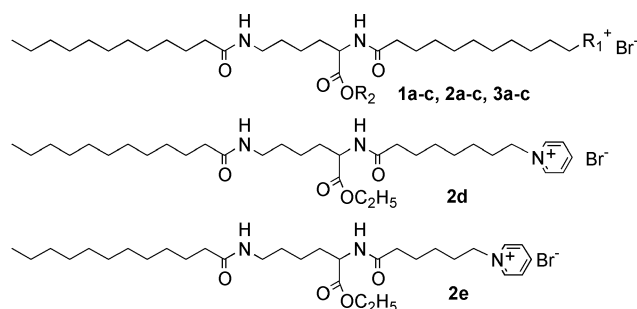
The results of the gelation test in water are listed in Table 1, giving the values of the mean minimum gel concentration

**Table 1** Gelation ability of 1–3 in water

	State <sup>a</sup>	MGC (mg ml <sup>-1</sup> )	H <sub>2</sub> O per gelator <sup>b</sup>
<b>1a</b>	TG	3 (4.5mM)	12300
<b>2a</b>	TG	3 (4.4mM)	12500
<b>3a</b>	WG	10 (12.6mM)	4400
<b>1b</b>	TG	5 (7.4 mM)	7460
<b>2b</b>	TG	5 (7.3 mM)	7600
<b>3b</b>	WG	10 (12.5 mM)	4440
<b>1c</b>	S		
<b>2c</b>	S		
<b>3c</b>	S		
<b>2d</b>	TLG	6 (9.4 mM)	5930
<b>2e</b>	S		

<sup>a</sup> Values mean minimum gel concentration necessary for gelation of water (mg ml<sup>-1</sup>) and its molar concentration. <sup>b</sup> The number of water molecules entrapped by one gelator molecule. TG: Transparent gel; TLG: Translucent gel; WG: White gel; S: Solution (at 5 wt%).

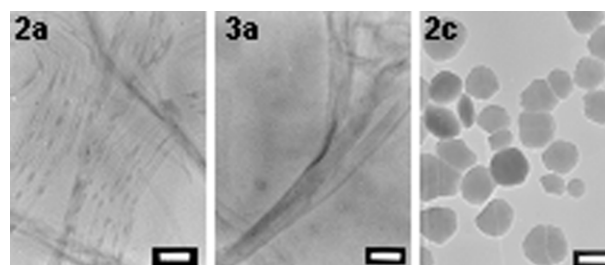
(MGC) necessary for gelation. **1a–3a**, **1b–3b**, and **2d** can form a hydrogel below 1 wt%; particularly, **1a** and **2a** can gel water at 0.3 wt% corresponding to more than 12000 water molecules/gelator. These hydrogels are very stable and keep the gel state for at least 4 months. In contrast, **1c–3c** and **2e** cannot gel water



R <sub>2</sub> \ R <sub>1</sub>	–N <sup>+</sup>	–N <sup>+</sup> –N(CH <sub>3</sub> )	–N(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> <sup>+</sup>
CH <sub>3</sub>	<b>1a</b>	<b>1b</b>	<b>1c</b>
C <sub>2</sub> H <sub>5</sub>	<b>2a</b>	<b>2b</b>	<b>2c</b>
C <sub>10</sub> H <sub>21</sub>	<b>3a</b>	<b>3b</b>	<b>3c</b>

even at 6 wt%. Furthermore, the gelation significantly depends on the length of the alkyl groups in the ester and alkylene spacer between the L-lysine segment and positively charged terminal; the gelation ability of **1a** and **2a** is superior to that of **3a** possessing a longer alkyl ester group and **2d** possessing a shorter alkylene spacer. These results suggest that the gelation of water using the L-lysine derivatives requires the quaternized aromatic heterocycle group, and an appropriate hydrophilic–hydrophobic balance in the gelator molecule.

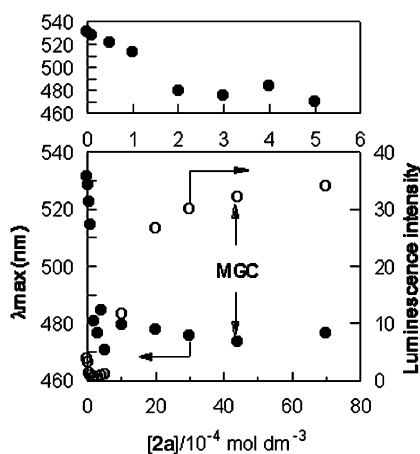
Fig. 1 shows TEM pictures of the samples prepared from **2a**, **3a**, and **2c** in water.‡ **2a** created three-dimensional (3D) networks by the entanglement of ca. 50–60 nm fine fibers in the hydrogels, while **3a** created a network structure by the ca. 100–200 nm nanoribbons. It is noteworthy that the nanostructure depends on the alkyl chain length in the ester. The 3D network structure is very similar to that observed in organogels. In contrast, **2c** formed spherical aggregates with diameters of



**Fig. 1** TEM images of samples of **1a**, **2a**, and **2c** formed in water. Scale bar is 200 nm.

ca. 200 nm.<sup>5</sup> This result indicated that the formation of the hydrogels requires the creation of the 3D network structures and the gelation of water formed by entrapping water molecules into the spaces of the 3D networks. Since the FTIR spectrum gives useful information on intermolecular hydrogen bonding interactions, we measured the FTIR spectra of the hydrogels in D<sub>2</sub>O<sup>6</sup> and no self-assembly gelators in CHCl<sub>3</sub>. The FTIR spectrum of **2a** in CHCl<sub>3</sub> demonstrates the absorption bands at 1660 cm<sup>-1</sup> (νC=O, amide I) and 1516 cm<sup>-1</sup> (δN-H amide II) assigned to the non-hydrogen bonding amide group, while in D<sub>2</sub>O, the absorption bands at 1630 cm<sup>-1</sup> (amide I) and 1540 cm<sup>-1</sup> (amide II) characterized the hydrogen bonded amide group. These results indicate that the gelator molecules undergo intermolecular hydrogen bonding in the nanofibers.

In order to analyze the gelation mechanism in more detail, the luminescence spectra of 8-anilino-1-naphthalenesulfonic acid (ANS) as a fluorescent probe were measured at various hydrogelator concentrations. Fig. 2 shows the dependence of the luminescence maxima (λ<sub>max</sub>) and luminescence intensity on the concentration of **2a**.<sup>7</sup> In the low concentration range, λ<sub>max</sub> was sharply blue-shifted and I/I<sub>0</sub> slightly decreased with the increasing concentration of the hydrogelators. However, as the I/I<sub>0</sub> increased, the λ<sub>max</sub> was almost constant. These results imply that **2a** already forms self-assemblies possessing hydrophobic domains (pockets) below the MGC. In addition, one of the driving forces for the self-organization of the gelators is a hydrophobic interaction.



**Fig. 2** Luminescence behavior of ANS ( $1.0 \times 10^{-5} \text{ mol dm}^{-3}$ ) in an aqueous solution containing various concentrations of **2a**. (○): luminescence intensity and (●): luminescence maxima ( $\lambda_{\text{max}}$ ).

In summary, we have developed low molecular weight gelators based on L-lysine derivatives that can be simply and effectively synthesized. These compounds can gel water below 1 wt%; particularly, **1a** and **2a** form a hydrogel at 0.3 wt%. The gelation of water is induced by entrapping water molecules into the spaces of the 3D networks created by entanglement of the self-assembled nanofibers, and the hydrogelators undergo not

only hydrophobic interactions but also intermolecular hydrogen bonding in the nanofibers.

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## Notes and references

† Gelation test: A mixture containing a known weight of gelator in water (1 ml) in a sealed test tube was heated at ca. 40 °C to a clear solution and then cooled to room temperature. After allowing the solutions to stand at 25 °C for 6 h, the state of the solution was evaluated.

‡ TEM: The TEM images were obtained using a JEOL JEM-2010 electron microscope at 200 kV. Samples were prepared as follows: the aqueous solutions of the gelators were dropped on a collodion- and carbon-coated 400 mesh copper grid and immediately dried *in vacuo* for 24 h. After dipping in a 1% phosphotungstic acid solution, the grids were dried under reduced pressure for 24 h.

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- Similar spherical aggregates were also observed for compounds **1c**, **3c**, and **2d**, which had no gelation ability for water.
- It is very difficult or almost impossible to obtain useful information on the hydrogen bonding interactions in an aqueous gel.
- The luminescence results for **1a**, **1b**, and **2b**, were similar to **2a**, and those for **1c**, **3c**, and **2e** were similar to **2c**. In contrast, the luminescence spectra of ANS in aqueous solutions of **3a**, **3b**, and **3c** could not be measured due to their opacity.