Letter

New low-molecular-weight hydrogelators based on L-lysine with positively charged pendant chain

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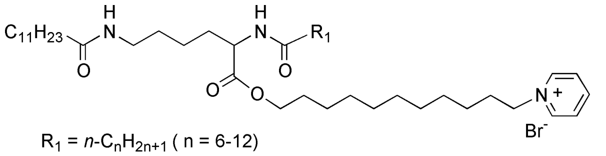
Received (in Montpellier, France) 19th February 2002, Accepted 8th April 2002
First published as an Advance Article on the web 31st May 2002

New low-molecular-weight gelators, L-lysine derivatives with a positively charged terminal in the ester group, can gel water at low concentrations; in particular, 1 and 8 form a hydrogel at 0.1 wt%.

Hydrogels have been extensively investigated because of their applications for tissue engineering[1] and development of new materials that reversibly response to various external stimuli.[2] They usually consist of covalently or noncovalently cross-linked polymers and contain a large amount of water that fills the interstitial spaces of the network. These hydrogels have complicated intermolecular association modes that are difficult to define. In contrast, since physical gels such as organogels and hydrogels, which are formed by low-molecular-weight compounds, are one-dimensional aggregates, the definition of the association modes is relatively easy. In spite of many reports on organogelators,[3] however, there are only a limited number of hydrogels formed by low-molecular-weight compounds.[4] Here we describe new low-molecular-weight hydrogelators **1**–**8** and their self-assembling behavior and gelation ability in water.



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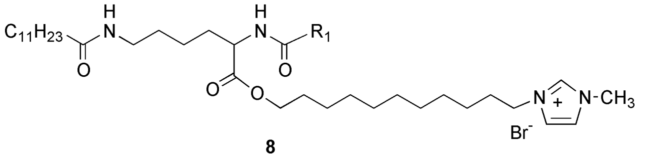

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The results of the gelation test and the values of the minimum gelation concentration (MGC) necessary for hydrogel formation are listed in Table 1. Except for **6**, these compounds have excellent gelation abilities for water and form a hydrogel. In particular, **1** and **8** form a hydrogel at 0.1 wt%. These hydrogels are very stable and maintain the gel state for at least 6 months. Very interestingly, the MGC values depend significantly on the length of the alkyl chain linked at the N^{α}-position; the gelation ability decreases with the increasing length of the alkyl chain. This is likely because steric hindrance affects the formation of the hydrogel. Furthermore, the hydrogels become opaque with increasing length of the alkyl chain; this is probably induced by an increase in the size of the nanostructure.

Table 1 Results of the gelation test of **1**–**8** in water

Compound	MGC[a]	H_2O/gelator[b]
1	1 (T)	41 000
2	3 (TL)	14 000
3	10 (O)	4300
4	13 (O)	3300
5	15 (O)	2900
6	S	
7	25 (O)	1800
8	1 (T)	41 000

[a] Minimum gel concentration necessary for gelation (mg ml^{-1}). T: transparent gel. TL: translucent gel. O: Opaque gel. S: Solution at 5 wt%. [b] The number of water molecules entrapped by a gelator molecule.

Fig. 1 shows TEM images of samples prepared from the hydrogels of **1** and **8**. In the hydrogels, these hydrogelators create a three-dimensional network, which is formed by entanglement of the fine fibers having diameters of *ca.* 15–20 nm. Therefore, the formation of the hydrogels is caused by entrapping water (solvent) molecules into the spaces of the network, like common organogels. On the other hand, the TEM image of the hydrogel of **7** shows *ca.* 100–200 nm nanofibers. Probably, the strong interactions between the long alkyl chains lead to preferable self-assembly into large nanofibers compared to **1** and **8**.

To evaluate the self-assembling behavior, we measured the fluorescence spectra of 8-anilino-1-naphthalenesulfonic acid (ANS) in an aqueous solution of **1** and the FTIR spectrum

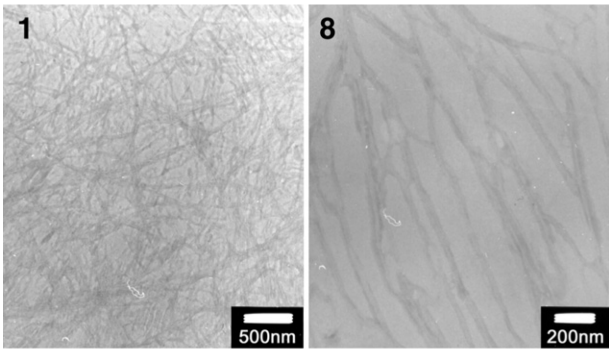

Fig. 1 TEM images of samples prepared from **1** and **8** in water.

DOI: 10.1039/b201847k

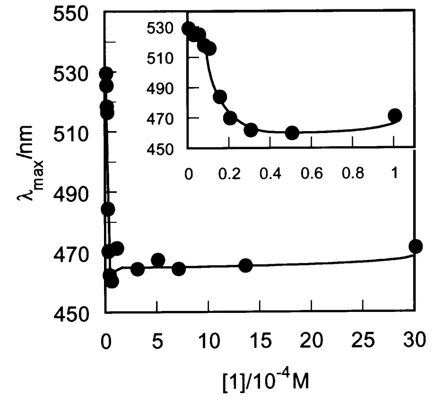

Fig. 2 Dependence of luminescence maxima of ANS on concentration of **1**. [ANS] = 1.0×10^{-5} M. Inset: blow-up of the low concentration range.

of the hydrogel of **1**. Fig. 2 shows the dependence of the luminescence maxima (λ_{max}) of ANS on the concentration of **1**. λ_{max} is blue-shifted up to 2.0×10^{-5} M and then remains almost constant, indicating that **1** begins to form some self-assembled structures having hydrophobic pockets at a concentration lower than MGC, and ANS is incorporated into the hydrophobic pockets (this self-assembly may be a spherical micelle)[5]. Namely, **1** self-assembles into a nanostructure through hydrophobic interactions.

Fig. 3 shows the FTIR spectra of **1** in chloroform and D_2O.[6] The FTIR spectrum in chloroform, in which no self-assembly occurs, shows absorption bands at 1658 and 1514 cm^{-1}, characteristic of non-hydrogen-bonded C=O (amide I) and N–H (amide II). In contrast, the FTIR spectrum in D_2O is characterized by bands at 1632 ($\nu_{C=O}$, amide I) and 1543 (δ_{N-H}, amide II) cm^{-1}, which are assigned to hydrogen-bonded amide groups.[7] This result indicates that **1** forms intermolecular hydrogen bonds in the nanofibers. Moreover, the antisymmetric (ν_{as}) and symmetric (ν_s) CH_2 stretching vibrational modes of **1** in D_2O shift to lower wavenumbers (2930 → 2920 cm^{-1} and 2857 → 2850 cm^{-1}) due to the decrease in the chain fluidity[8] induced by hydrophobic interactions between alkyl groups.

In summary, we have described new low-molecular-weight hydrogelators based on L-lysine. The compounds have an excellent gelation ability for water; in particular, **1** and **8** can gel water at 0.1 wt%. The FTIR, TEM, and fluorescence measurements indicate that spherical micelles are formed at first (below MGC) through hydrophobic interactions; these then aggregate to form nanofibers upon cooperative formation of hydrogen bonds. Then entanglement of the nanofibers creates a three-dimensional network structure, which leads to hydrogel formation.

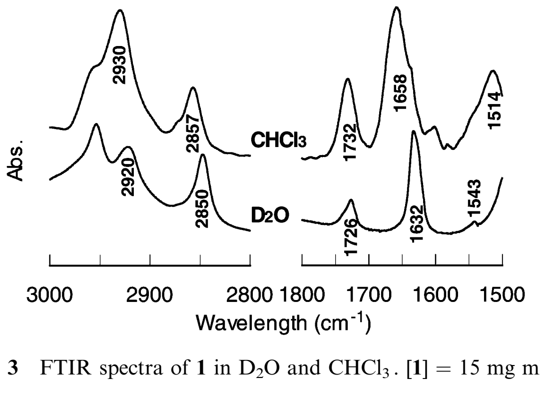

Fig. 3 FTIR spectra of **1** in D_2O and $CHCl_3$. [**1**] = 15 mg ml^{-1}.

Experimental

Compounds **1**–**8** were prepared from commercially available N^{ε}-lauroyl-L-lysine from the Ajinomoto Co., Ltd., according to a synthetically simple approach: esterification by 11-bromoundecanol (80% yield), acylation by *n*-bromoalkanoyl chloride (98% yield), and then quaternization (95% yield). The gelation ability of these compounds was evaluated by the stable-to-inversion method of a test tube after allowing the solutions to stand at room temperature for 6 h followed by dissolution into water with mild heating.

Acknowledgements

This work was supported by a Grant-in-Aid for COE Research (10CE2003) by the Ministry of Education, Culture, Sports, Science, and Technology of Japan and The Kao Foundation for Arts and Science.

Notes and references

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6 Since it is very difficult to obtain useful information about the intermolecular hydrogen-bonding interaction of **1** in H_2O from the FTIR study, we used D_2O as the solvent.

7 These absorbances almost linearly depend on the concentration of **1**.

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