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L-Lysine-based supramolecular hydrogels containing various inorganic ions

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The preparation of supramolecular hydrogels containing various inorganic acids and salts using L-lysine-based hydrogelators is conducted and their thermal stabilities, gel strengths, FT-IR spectra, and electron micrographs are measured. These hydrogelators can form supramolecular hydrogels over a wide pH range and contain inorganic acids and salts. The supramolecular hydrogels based on ester-type hydrogelators have good thermal stabilities (high T_{gel}), while the hydrogelator with a carboxyl group forms a thermally sensitive gel with high mechanical strength. Furthermore, the gelation mechanism is discussed using FT-IR spectroscopy and TEM observations.

Introduction

In supramolecular chemistry, many self-assembled architectures have been produced through non-covalent interactions.[1] For instance, new types of liquid crystal materials and organogels have been found by arrangement of multiple hydrogen bonding.[2,3] In particular, gelation phenomena by low-molecular-weight compounds through supramolecular interactions such as hydrogen bonding, van der Waals, π-stacking, and coordination interactions have attracted much attention.[2,4] Such organogels are new soft materials that have many potential applications, *e.g.* gel electrolytes,[5] sensors,[6] and organic templated materials.[7]

On the other hand, hydrogels have been extensively investigated because of their potential applications for superabsorption, drug delivery materials, and tissue engineering scaffolds and the development of new materials that reversibly respond to various external stimuli.[8,9] They have been traditionally constructed with high molecular weight, hydrophilic polymers that are physically cross-linked through entanglements or chemically cross-linked into a network, and contain a large amount of water that fills the interstitial spaces of the network. Recently, the construction of hydrogels by low-molecular-weight compounds (hydrogelators) has been explored.[10–12] Such hydrogelators self-assemble into nanostructures (fibers, ribbons, tapes, sheets, *etc.*) and then produce gel networks with tunable, responsive properties.

We have focused on the self-assembling properties of organogelators in organic solvents and converted them into hydrogelators. One of the successful examples is L-lysine-based hydrogelators obtained by the introduction of charged groups such as positively charged pyridiniums and imidazoliums as well as a negatively charged carboxylate.[13] Especially, the positively charged L-lysine derivatives can gel pure water at 0.3 wt%. In order to use hydrogelators in many fields, hydrogenation ability should be investigated under various conditions (*e.g.* pHs, ionic strengths, *etc.*). We now describe hydrogelation in aqueous solutions containing inorganic salts and acids, saline, and buffer solutions.

Results and discussion

pH effects

Table 1 Effects of pH on hydrogelation of **1–3**[a]

	HCl/NaOH[b]			Buffer[c]		
pH	1	2	3	1	2	3
0	7	3	1	—	—	—
1	6	6	2	—	—	—
2	6	7	9	7	3	1
3	6	12	10	5	3	1
4	6	15	10	4	15	1
5	5	15	10	3	PG	3
6	5	15	12	3	PG	3
7	3[d]	15[d]	12[d]	3	S	3
8	5	17	12	3	S	5
9	5	17	15	3	S	5
10	5	17	15	5	S	20
11	6	17	20	VS	S	30
12	25	25	VS	S	S	PG
13	S	S	VS	—	—	—
14	S	S	S	—	—	—

[a] Values denote minimum gelation concentration necessary for hydrogel formation (g L^{-1}). [b] pH values were calculated from the amount of added HCl (pH 1–6) and NaOH (pH = 8–14). [c] pH values were adjusted using a Carmody buffer. [d] In pure water. VS: viscous solution at 50 g L^{-1}. S: solution at 50 g L^{-1}. PG: partial gel at 50 g L^{-1}.

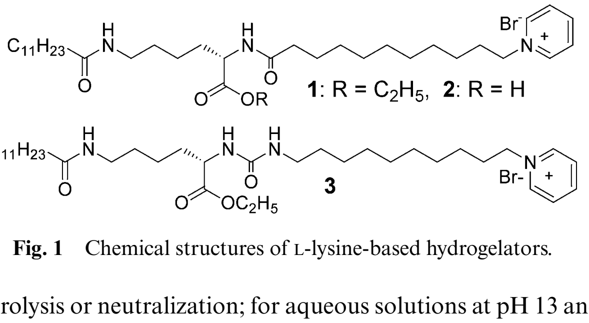

Fig. 1 Chemical structures of L-lysine-based hydrogelators.

The hydrogelation properties of **1–3** (Fig. 1) are listed in Table 1, where the values mean minimum gel concentration (MGC; g L^{-1}) necessary for hydrogel formation. None of the compounds could gel a strong alkali solution because of hydrolysis or neutralization; for aqueous solutions at pH 13 and 14, the ester groups in **1** and **3** were hydrolyzed during heating to dissolve gelators in the solutions and the carboxylic acid group in **2** changed to carboxylate (CO_2^- Na^+). In pure water (pH = 7), **1** showed the best hydrogelation ability, forming a hydrogel at 3 g L^{-1}, while the MGC values of **2** and **3** are 15 g L^{-1} and 12 g L^{-1}. For **1**, the smallest MGC value is obtained in pure water (pH = 7) and the hydrogelation ability decreased with increasing alkalinity and acidity. Thus, **1** can form hydrogels in aqueous solutions with wide pH ranges below pH 11. In contrast,

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although **2** and **3** showed good hydrogelation abilities for aqueous solutions of a low pH, their hydrogelation abilities decreased with increasing pH; especially, **3** gelled an aqueous solution of pH = 0 at 1 g L^{-1}, and the hydrogelation ability was *ca.* 12 times better than that in pure water.

After dissolution of **1** and **3** into aqueous solutions adjusted to each pH, the pH of the solution will hardly change because the hydrogelators do not have a pH-responsive functional group. In contrast, the dissociation of the carboxylic acid group in **2** depends on pH. Below pH <7, however, the pHs are adjusted by addition of HCl_{aq} and pure water (pH = 7), which is almost ion-free, leading to no dissociation of the carboxylic acid group. At pH >7, the aqueous solutions include NaOH and an acid–base reaction will occur. In the control experiment, the sodium salt of **2** had no hydrogelation property.[14] This fact indicates that **2** maintains the carboxylic acid form even in an aqueous solution containing 10 mM NaOH (corresponding to pH = 12); indeed, the FT-IR spectrum of **2** in D_2O solution containing 10 mM NaOD showed the IR peak corresponding to the stretching vibration of CO_2H (νC=O) around 1720 cm^{-1}.

The hydrogelation properties of **1–3** were examined in aqueous solutions with various pHs adjusted using a Carmody buffer.[15] Carmody buffer, which consists of 0.2 M boric acid, 0.05 M citric acid, 0.1 M trisodium phosphate, and pure water, is very useful because it can be adjusted within a wide pH range (pH 2–12) by changing their ratios.[15] As listed in Table 1, **2** lost its hydrogelation property over pH = 4. In addition, **2** cannot gel the aqueous solutions with pH = 4 and 5 adjusted using a CH_3CO_2H–CH_3CO_2Na buffer (data not shown). Considering the lack of hydrogelation ability of the sodium salt of **2**, most of the carboxylic acid groups in **2** change to the carboxylate form ($CO_2H \rightarrow CO_2^- Na^+$) in buffer solutions over pH = 4; probably, in the buffer solutions, many citrate (Carmody buffer) and acetate (acetate buffer) ions accelerate the proton-dissociation of **2**. In contrast, **1** and **3** show similar hydrogelation behavior while their hydrogelation abilities increase; *e.g.*, the MGC values of **3** at pH = 2–4 are 1 g L^{-1} and the hydrogelation abilities are *ca.* 10 times larger. It is likely that the many ions in the buffer solution influence hydrogelation.

Effects of salts and acids

In order to examine the influence of ions contained in an aqueous solution on hydrogelation, hydrogelation tests were carried out in aqueous solutions containing various salts and acids. The hydrogelation properties of **1–3** in water, saline, and aqueous solutions containing various acids and inorganic salts are listed in Table 2. The hydrogelation ability of **1** in saline and aqueous solutions containing 1 M CH_3CO_2H, NaCl, and KCl and 0.1 M $MgCl_2$, and $CaCl_2$ nearly equalled that in pure water, while it decreased in aqueous acid solutions. This result indicates that the hydrogelation ability of **1** in Carmody buffer (pH = 4–9) is increased by high ionic strength. **2** and **3** efficiently gel aqueous solutions of inorganic acids and salts, compared with pure water, although their hydrogelation abilities in 1 M acetic acid solution are similar to those in pure water. In addition, **3** can also form a hydrogel in an aqueous solution containing 4 M HCl at 0.7 wt% that **1** and **2** never gel. These results indicate that the hydrogelation behavior of **1** hardly depends on additives (such as inorganic acids and salts), while the presence of inorganic salts and acids affects hydrogelation of **2** and **3** and enhances their hydrogelation abilities. It is well known that the hydrophilic–hydrophobic balance in the gelator molecule is important for the formation of a supramolecular hydrogel.[10] **1** has an excellent balance, but **2** and **3** may be unbalanced (resulting in low MGC values for pure water). The change in polarity of an aqueous solution by the addition of inorganic salts and acids may compensate for their imbalance; consequently, the hydrogelation abilities of **2** and **3** are similar to that of **1**.

On the other hand, for **2** and **3**, the MGC values in pure water are very large compared with those in aqueous solutions containing inorganic acids and salts. We tried the formation of hydrogels at room temperature. When aqueous solutions of inorganic salts and acids were rapidly added to an aqueous solution of **2** or **3** at 0.8 wt%, hydrogelation occurred immediately. Though the hydrogels obtained are partly heterogeneous, they become homogeneous gels after heating–dissolution.

Aspects of hydrogels and TEM

Fig. 2 shows photographs of hydrogels prepared from **2** and **3** in pure water and 1 M HCl solutions at the MGC. **1** forms a transparent hydrogel in pure water[4c] and other aqueous solutions at the MGC. In pure water, the hydrogels of **2** (A) and **3** (C) are translucent. **2** also forms translucent hydrogels in saline and 1 M CH_3CO_2H and transparent ones in other solutions (photo B in 1 M HCl). In contrast, although the 1 M HCl (photo D) and 1 M H_2SO_4 gels of **3** are transparent, **3** forms slightly cloudy (almost transparent) gels in other solutions. This aspect of the hydrogels arises from a difference in the MGC values. The transparent hydrogels were formed at low MGC values, while the translucent hydrogels were formed when the MGC values were large. Indeed, these hydrogelators form a translucent hydrogel at a high concentration in aqueous solutions that form a transparent hydrogel at MGC.

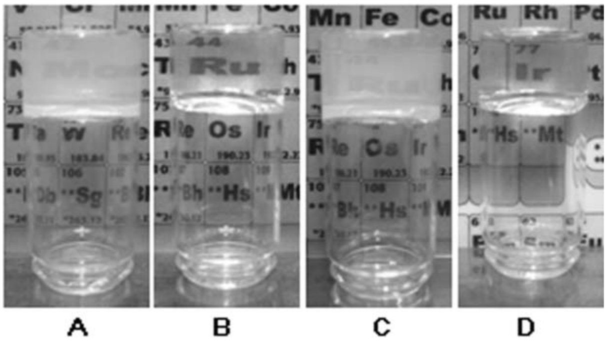

Fig. 2 Photographs of hydrogels prepared from **2** and **3**. A: **2** in pure water (15 mg ml^{-1}); B: **3** in pure water (12 mg ml^{-1}); C: **2** in 1 M HCl (3 mg ml^{-1}); D: **3** in 1 M HCl (1 mg ml^{-1}).

Hydrogelators often self-assemble into nanofibers with very small diameters in transparent hydrogels; *e.g.*, the self-assembled nanofibers of **1** in pure water have a diameter of *ca.* 16 nm.[4c] Superstructures built up with **2** and **3** in hydrogels were observed by transmission electron microscopy (TEM). Fig. 3 shows TEM photographs of the dried hydrogels of **2** and **3** prepared in pure water and 1 M HCl. As expected, these gelators form nanofibers

Table 2 Hydrogelation properties of **1–3** in water, saline, and aqueous solutions containing inorganic salts and acids (1 mol dm^{-3})[a]

	H_2O	Saline	HCl	H_2SO_4	H_3PO_4	AcOH	NaCl	KCl	$MgCl_2$	$CaCl_2$
1	3[b]	4	7	6	5	2	4	3	4	5
2	15	15	3	3	6	16	2	3	4	4
3	12	7	1	1	3	12	4[c]	4[c]	6[c]	9[c]

[a] Values denote minimum gel concentration necessary for hydrogel formation (g L^{-1}). [b] Ref. 4*a*. [c] [NaCl] = [KCl] = [$MgCl_2$] = [$CaCl_2$] = 0.1 mol dm^{-3}.

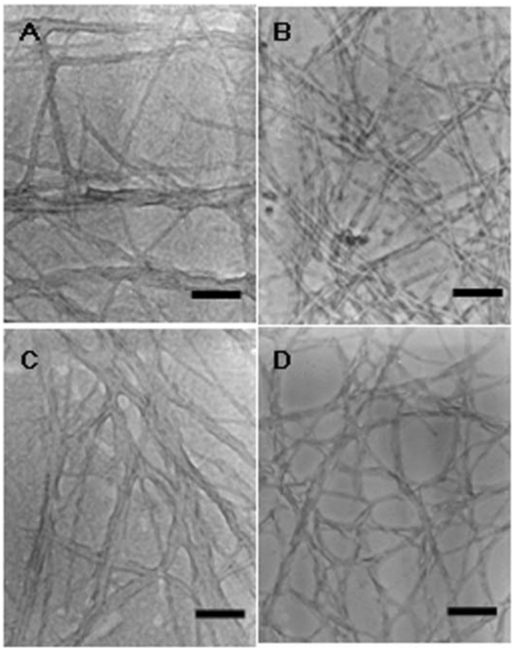

Fig. 3 TEM images of dried hydrogels prepared from **2** and **3**. A: **2** in pure water (15 mg ml^{-1}); B: **3** in pure water (12 mg ml^{-1}); C: **2** in 1 M HCl (3 mg ml^{-1}); D: **3** in 1 M HCl (1 mg ml^{-1}).

with a diameter of *ca.* 20 nm in transparent 1 M HCl gel. In translucent hydrogels (pure water), **2** and **3** self-assemble into nanofibers with wide diameter ranges (20–100 nm).

Hydrogel-destroyed temperatures (T_{gel})

Fig. 4 shows the hydrogel-destroyed temperatures (T_{gel}) of hydrogels based on **1**, **2** and **3** in pure water as a function of concentration, and the T_{gel} values for hydrogels formed at 20 g L^{-1} of gelator in various aqueous solutions are listed in Table 3. T_{gel} values are determined by an inversion-stable method in a concentration range from the MGC to 50 g L^{-1} of gelator. For **1** and **2**, T_{gel} increases as the concentration of gelator increases. The T_{gel} values are 50 °C at 30 g L^{-1} for **1** and 35 °C at 50 g L^{-1} for **2**. In contrast, **3** forms a thermally stable hydrogel; T_{gel} is given by 60 °C at 25 g L^{-1} for **3**. It is noteworthy that T_{gel} values change drastically from 25 °C to 50 °C in the small concentration range for **3** (15 g L^{-1} to 17 g L^{-1}). Generally, gelators possessing urea groups form bifurcated hydrogen bonds in nanofibers with thermal stability.[16] It may be the existence of the gelator concentration that accelerates the bifurcated hydrogen bonding interaction (induces cooperative effect).

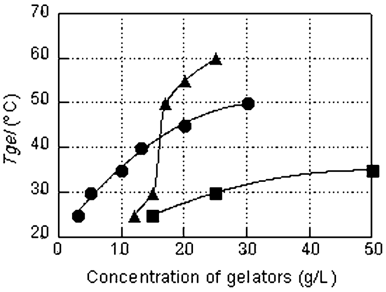

Fig. 4 T_{gel} for hydrogels of **1** (●), **2** (■), and **3** (▲).

As listed in Table 3, the thermal stabilities of hydrogels depend on the gelators; the T_{gel} values for hydrogels at 20 g L^{-1} of gelator show 45 °C for **1**, 27 °C for **2**, and 55 °C for **3**. It is clear that hydrogels based on **3** have the best thermal stabilities and that hydrogels of **2** have low thermal stabilities. As mentioned above, the strong bifurcated hydrogen bonding between the urea groups contributes to the high thermal stabilities of the hydrogels based on **3**. **1** has two potential hydrogen bonding sites (two amide groups),[17] while **2** has three potential hydrogen bonding sites (two amide groups and a carboxylic acid group). Shinkai and coworkers propose that a 1D hydrogen bonded network promotes gelation whereas 2D and 3D networks produce a weak gel.[18] Although **2** has better potential hydrogen bonding sites than **1** and **3**, **2** should form 2D or 3D networks due to the carboxylic acid group capable of hydrogen bonding, leading to the formation of hydrogels with low thermal stabilities.

On the other hand, the thermal stabilities of hydrogels increase in the presence of inorganic ions except for acetic acid, which hardly affects the T_{gel}. For **1**, the thermal stabilities of the hydrogels containing inorganic ions are larger than that of pure water; especially, the T_{gel} values of hydrogels based on **1** containing 1 M NaCl and 1 M KCl increase by 12 °C below 10 g L^{-1} (1 wt%) at 55 °C. The 0.1 M $CaCl_2$ hydrogel formed by **3** is the most thermally stable and is given by T_{gel} = 65 °C at 15 g L^{-1}.

FT-IR studies

Fig. 5 shows the temperature-controlled FT-IR spectra of **2** in D_2O. Up to 35 °C (hydrogel), the absorption bands were observed at 1724 cm^{-1} (carboxyl, νC=O) and 1634 cm^{-1} (amide I, νC=O), characteristic of hydrogen bonded carboxyl and amide groups. By increasing the temperature to 40 °C, the hydrogel was broken and the IR spectra dramatically changed; the absorption band of the amide I decreased and that of the carboxyl group decreased and shifted to a lower wavenumber (1724 cm^{-1} → 1717 cm^{-1}). In addition, the absorption around 1650 cm^{-1} corresponding to the non-hydrogen bonded amide I increased.

On the other hand, the absorption bands of the antisymmetric (ν_{as}) and symmetric (ν_s) CH_2 stretching vibrations of **2** appeared at 2922 cm^{-1} (ν_{as}, C–H) and 2850 cm^{-1} (ν_s, C–H) up to 35 °C,

Table 3 T_{gel} values and gel strengths of hydrogels based on **1–3** in aqueous solutions[a]

	1		2		3	
	T_{gel}	Strength/kPa	T_{gel}	Strength/kPa	T_{gel}	Strength/kPa
H_2O	45 °C	0.89	27 °C	12.91	55 °C	0.72
Saline	53 °C	1.26	32 °C	53.06	57 °C	7.53
1 M HCl	48 °C	4.12	37 °C	26.89	57 °C	23.84
1 M H_2SO_4	50 °C	5.37	42 °C	66.15	57 °C	19.54
1 M H_3PO_4	50 °C	11.47	42 °C	104.17	57 °C	8.42
1 M CH_3CO_2H	36 °C	39.62	25 °C	2.15	55 °C	1.79
1 M NaCl	57 °C	5.01	45 °C	77.98	60 °C[b]	8.25[b]
1 M KCl	57 °C	2.87	45 °C	26.00	60 °C[b]	23.84[b]
0.1 M $MgCl_2$	50 °C	5.02	42 °C	52.17	62 °C	19.18
0.1 M $CaCl_2$	50 °C	3.77	42 °C	83.90	62 °C	28.14

[a] [Gelator] = 20 g L^{-1}. [b] [NaCl] = [KCl] = 0.1 M. Agar: 43.75 kPa (20 g L^{-1}).

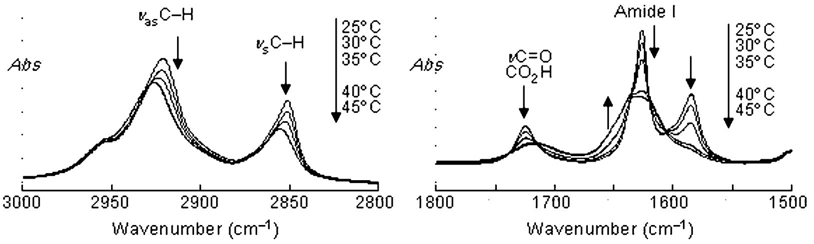

Fig. 5 Temperature-controlled FT-IR spectra of **2** (50 mg ml^{-1}) in D_2O.

while over 35 °C, they shifted to 2927 cm^{-1} and 2857 cm^{-1}. It is well known that a higher frequency shift of IR bands arising from alkyl chains is induced by an increase in the fluidity of the alkyl chains.[7] Probably, the alkyl chains in **2** strongly interacted *via* hydrophobic interactions in the hydrogel. For all hydrogels, such dramatic IR spectral changes were observed around T_{gel}. The IR results indicate that the gel-to-sol transition is induced by breaking hydrogen bonds and van der Waals (hydrophobic) interactions.

Gel strength

The strengths of the hydrogels formed at 20 g L^{-1} are listed in Table 3. The strengths of the hydrogels increased in the presence of inorganic salts and acids. In pure water, the strength of the hydrogel based on **3** was similar to that of **1**, while in the presence of inorganic salts and acids, the gel strength of **3** was large except in the presence of acetic acid and phosphoric acid. This may be attributed to the effect of the strong hydrogen bond of the urea groups in **3**, which is supported by the high T_{gel} of **3**. Interestingly, **2** formed the most rigid hydrogel among **1**–**3**, although it showed the smallest hydrogelation abilities and thermal stabilities; especially, the strength of the CH_3CO_2H gel based on **2** was *ca.* 100 kPa that was more than 40 times larger than that of pure water. This is attributed to the fact that 2D and 3D hydrogen bonding networks created by **2** lead to the formation of an elastic (rigid) hydrogel.[18] Therefore, **2** forms thermally sensitive hydrogels with strong mechanical strength.

Experimental

Materials

N^{ε}-Lauroyl-L-lysine was obtained from the Ajinomoto Co., Inc. N^{ε}-Lauroyl-N^{α}-(11-pyridiniumundecanoyl)-L-lysine ethyl ester (**1**) was prepared using a previously reported method.[13a] 10-Bromodecyl isocyanate was synthesized from 11-bromoundecanoyl chloride as a starting material according to the literature.[19] The other chemicals were of the highest commercial grade available and used without further purification. All solvents used in the syntheses were purified, dried, or freshly distilled as required.

Synthesis

N^{ε}-Lauroyl-N^{α}-(11-bromoundecanoyl)-L-lysine. N^{ε}-Lauroyl-L-lysine (60 mmol) was dissolved in water (500 ml) containing NaOH (300 mmol) and ethyl ether (300 ml) was added. 11-Bromoundecanoyl chloride was added to the ether layer. The biphasic solution was vigorously stirred at 0 °C for 1 h and an additional 23 h at room temperature. The resulting solution was carefully acidified by conc. HCl (pH $\approx$1). The white precipitate was filtered and washed with water. The product was obtained by two recrystallizations from ethanol–ether (85%). IR (KBr): 3304 cm^{-1} (νN–H, amide A), 1713 cm^{-1} (νC=O, CO_2H), 1643 cm^{-1} (νC=O, amide I), 1557 cm^{-1} (νN–H, amide II); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS, 25 °C): $\delta = 0.88$ (t, $J =$ 6.6 Hz, 6H; CH_3), 2.18 (t, $J = 7.3$ Hz, 2H; N^{ε}HCOCH_2), 2.25 (t, $J = 7.3$ Hz, 2H; CH_2CON$^{\alpha}$H), 3.15–3.33 (m, 2H; N^{ε}HCH_2), 3.40 (t, $J = 6.8$ Hz, 2H; CH_2Br), 4.50–4.55 (m, 1H; CH), 6.01 (t, $J = 5.8$ Hz, 2H; $N^{\varepsilon}H$), 6.77 (d, $J = 7.8$ Hz, 2H; $N^{\alpha}H$), 9.04 (br, 1H; CO_2H); elemental analysis calcd (%) for $C_{29}H_{55}BrN_2O_4$ (575.66): C, 60.51; H, 9.63; N, 4.87. Found: C, 60.55; H, 10.14; N, 4.87.

N^{ε}-Lauroyl-N^{α}-(10-bromodecylaminocarbonyl)-L-lysine ethyl ester. To a dry toluene solution (300 ml) of N^{ε}-lauroyl-L-lysine ethyl ester (20 mmol), 10-bromodecyl isocyanate (22 mmol) was added. The mixed solution was heated at 100 °C for 10 min. The resulting solution was evaporated to dryness. The product was obtained by recrystallization from ethanol–ether (96%). IR (KBr): 3339 cm^{-1}, 3292 cm^{-1} (νN–H), 1732 cm^{-1} (νC=O, ester), 1638 cm^{-1} (νC=O, amide I), 1621 cm^{-1} (νC=O, urea), 1550 cm^{-1} (νN–H, amide II); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS, 25 °C): $\delta = 0.88$ (t, $J = 6.6$ Hz, 6H; CH_3), 2.16 (t, $J = 7.3$ Hz, 2H; N^{ε}HCOCH_2), 3.13–3.18 (m, 2H; N^{α}HCONHCH_2), 3.20–3.26 (m, 2H; N^{ε}HCH_2), 3.40 (t, $J = 6.8$ Hz, 2H; CH_2Br), 4.17 (q, $J = 7.3$ Hz, 2H; OCH_2), 4.40–4.45 (m, 1H; CH), 4.94 (t, $J = 5.8$ Hz, 1H; N^{α}HCONH), 5.37 (d, $J = 7.8$ Hz, 1H; $N^{\alpha}H$), 5.91 (t, $J = 5.3$ Hz, 1H; $N^{\varepsilon}H$); elemental analysis calcd (%) for $C_{31}H_{60}BrN_3O_4$ (618.73): C, 60.18; H, 9.77; N, 6.79. Found: C, 60.22; H, 10.13; N, 6.80.

N^{ε}-Lauroyl-N^{α}-(11-pyridiniumundecanoyl)-L-lysine bromide (2). A pyridine solution (200 ml) of N^{ε}-lauroyl-N^{α}-(11-bromoundecanoyl)-L-lysine (50 mmol) was heated at 100 °C for 24 h under a nitrogen atmosphere. The resulting solution was evaporated to dryness. The product was obtained by recrystallization from ethanol–ether (98%). IR (KBr): 3414 cm^{-1}, 3307 cm^{-1} (νN–H, amide A), 1732 cm^{-1} (νC=O, CO_2H), 1642 cm^{-1} (νC=O, amide I), 1550 cm^{-1} (νN–H, amide II); ^{1}H-NMR (400 MHz, DMSO-d_6, TMS, 25 °C): $\delta = 0.86$ (t, $J =$ 6.6 Hz, 6H; CH_3), 2.05 (t, $J = 7.3$ Hz, 2H; N^{α}HCOCH_2), 2.12 (t, $J = 7.3$ Hz, 2H; CH_2CON$^{\varepsilon}$H), 3.03 (q, $J = 6.3$ Hz, 2H; N^{ε}HCH_2), 4.13–4.19 (m, 1H; CH), 4.66 (t, $J = 7.3$ Hz, 2H; CH_2Py$^+$), 7.68 (t, $J = 5.6$ Hz, 1H; $N^{\varepsilon}H$), 7.86 (d, $J = 7.8$ Hz, 1H; $N^{\alpha}H$), 8.17 (t, $J = 7.2$ Hz, 2H; 3-PyH), 8.62 (t, $J = 7.8$ Hz, 1H; 4-PyH), 9.18 (d, $J = 5.6$ Hz, 2H; 2-PyH); elemental analysis calcd (%) for $C_{34}H_{60}BrN_3O_4$ (654.76): C, 62.37; H, 9.24; N, 6.42. Found: C, 62.41; H, 9.64; N, 6.41.

N^{ε}-Lauroyl-N^{α}-(10-pyridiniumdecylaminocarbonyl)-L-lysine ethyl ester bromide (3). The product was obtained by the same procedure as **2** (95%). IR (KBr): 3365 cm^{-1}, 3293 cm^{-1} (νN–H), 1732 cm^{-1} (νC=O, ester), 1638 cm^{-1} (νC=O, amide I), 1623 cm^{-1} (νC=O, urea), 1550 cm^{-1} (νN–H, amide II); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS, 25 °C): $\delta = 0.87$ (t, $J =$ 6.6 Hz, 6H; CH_3), 2.22 (t, $J = 7.1$ Hz, 2H; CH_2CON$^{\varepsilon}$H), 3.08–3.25 (m, 4H; N^{α}HCONHCH_2, N^{ε}HCH_2), 4.08–4.14 (m, 2H; OCH_2), 4.28–4.34 (m, 1H; CH), 4.97 (t, $J = 7.3$ Hz, 2H; CH_2Py$^+$), 6.07 (t, $J = 5.3$ Hz, N^{α}HCONH), 6.41 (d, $J =$ 7.1 Hz, 1H; $N^{\alpha}H$), 6.63 (t, $J = 5.6$ Hz, 1H; $N^{\varepsilon}H$), 8.18 (t, $J =$ 7.2 Hz, 2H; 3-PyH), 8.53 (t, $J = 7.8$ Hz, 1H; 4-PyH), 9.52 (d, $J = 5.6$ Hz, 2H; 2-PyH); elemental analysis calcd (%) for $C_{36}H_{65}BrN_4O_4$ (697.83): C, 61.96; H, 9.39; N, 8.03. Found: C, 61.99; H, 9.64; N, 8.04.

Apparatus for measurements

Elemental analyses were performed using a Perkin-Elmer series II CHNS/O analyzer 2400. The VT-FT-IR spectra were recorded on a JASCO FS-420 spectrometer. TEM images were obtained using a JEOL JEM-2010 electron microscope at 200 kV. ^{1}H-NMR spectra were measured using a Bruker AVANCE 400 spectrometer with TMS as the standard. The strengths of hydrogels were measured using a Sun science Rheo Tex SD-305.

Gelation test

A mixture of a weighed gelator in water (1 ml) in a sealed test tube (14 mm in diameter) was heated at *ca.* 40 °C until a clear solution appeared. After allowing the solution to stand at 25 °C for 6 h, the state of the solution was evaluated by the "stable to inversion of a test tube" method.

Transmission electron micrograph (TEM)

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 a vacuum for 24 h. After dropping a 2 wt% phosphotungstic acid solution, the grids were dried under reduced pressure for 24 h.

Gel strength

Samples were prepared as follows: a mixture of a weighed gelator in water (2 ml) in a sealed sample tube (15 mm in diameter) was heated until a clear solution appeared. The gel strength was evaluated as strength necessary to sink a cylinder bar (8.35 mm in diameter) 4 mm deep in the gel.

FT-IR study at room temperature

FT-IR spectroscopy was performed in D_2O operating at a 2 cm^{-1} resolution with 32 scans. A spectroscopic cell with a CaF_2 window and 25 μm spacers was used for the measurements.

Temperature-controlled FT-IR study

An automatic temperature-control cell unit (Specac Inc., P/N 20730) with a vacuum-tight liquid cell (Specac Inc., P/N 20502, path length 50 μm) fitted with CaF_2 windows was used to measure the IR spectra at different temperatures.

Conclusion

We revealed the formation of supramolecular hydrogels of **1–3** in aqueous solutions containing inorganic salts and acids and the thermal properties of their hydrogels. These hydrogelators have hydrogelation abilities for aqueous solutions with a wide pH range and can form supramolecular hydrogels containing various ions such as Na^+, K^+, Mg^{2+}, Ca^{2+}, and H^+. The temperature-controlled FT-IR spectra demonstrate that the T_{gel} value is consistent with temperatures at which hydrogen bonding and van der Waals interactions are broken. Hydrogelator **3** possessing an urea bond forms the most thermo-stable hydrogel, while **2** with a carboxyl group shows the smallest T_{gel} value. In contrast, the supramolecular hydrogel based on **2** has the most mechanical strength compared with other hydrogelators; namely, **2** forms a thermo-sensitive hydrogel with high mechanical strength.

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