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Supramolecular hydrogels and organogels based on novel L-valine and L-isoleucine amphiphiles

Masahiro Suzuki,[a,*] Sanae Owa,[b] Mutsumi Kimura,[b] Akio Kurose,[c] Hirofusa Shirai[b] and Kenji Hanabusa[a]

[a]*Graduate School of Science and Technology, Shinshu University, Ueda, Nagano 386-8567, Japan*
[b]*Department of Functional Polymer Science, Faculty of Textile Science and Technology, Shinshu University, Ueda, Nagano 386-8567, Japan*
[c]*Aichi Konan College, Konanan 483-8086, Japan*

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Abstract—New low-molecular-weight gelators based on L-valine and L-isoleucine gelators, which have a positively charged terminal group, can gel not only pure water and aqueous solutions containing inorganic acids and salts but also some organic solvents and oils.

On the basis of supramolecular chemistry, functional low-molecular-weight compounds have been developed.[1] In particular, the compounds that self-organize into nano-scaled superstructures such as nanofibers, nanoribbons, nanoparticles, and helical structures are attractive.[1] Some compounds often gel various solvents, and are so-called hydrogelators for water[2] as well as organogelators for organic solvents.[3] Especially, organogelators have gained much attention not only for their organogelation properties but also the nano-scaled superstructures created in organogels; for example, the use as organic templates for the fabrication of mesoporous polymer materials[4] and nano-scaled designed inorganic materials[1c,5] and the application to liquid crystalline,[6] photochemistry,[7] and electrochemistry.[8]

We have also developed some organogelators and hydrogelators based on L-amino acids such as L-valine, L-isoleucine, and L-lysine.[8a,9] One of our main strategies is the transformation of organogelators into hydrogelators. Because hydrogelators can be designed with the self-assembling properties of organogelators, their synthetic procedures are very simple. Indeed, the L-lysine derivatives obtained by introduction of a positive charge into the L-lysine-based organogelators function as excellent hydrogelators that can gel water around 0.3 wt %.[9b] Unfortunately, the positively charged L-lysine hydrogelators lose their organogelation abilities. Gelators with an amphiphilic gelation property that can gel not only aqueous solutions but also organic solvents and oils are very useful materials because they will gel oil/water mixtures and undergo their selective gelation of oil or water from oil/water mixtures.[10] We now describe the synthesis of new positive charged L-valine and L-isoleucine derivatives and their gelation abilities in aqueous solutions and organic solvents.

Compounds **1** and **2** were prepared from octadecylamide compounds of Z-L-valine and Z-L-isoleucine.[†] The

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[†] L-Valylaminooctadecane (L-C_{18}ValNH$_2$) and L-isoleucylaminooctadecane (L-C_{18}IleNH$_2$) were prepared by deprotection of carbobenzyloxy group from *N*-carbobenzyloxy-L-valylaminooctadecane and *N*-carbobenzyloxy-L-isoleucylaminooctadecane.[8a] *N*-6-Halohexanoyl-L-valylaminooctadecane: to a dry THF solution of L-C_{18}ValNH$_2$ (20 mmol) and NEt$_3$ (10 mL), a freshly distilled 6-halohexanoyl chloride was slowly added at 0 °C with stirring and then the reaction mixture was stirred at room temperature for 12 h. The resulting solution was filtered and the filtrate was evaporated to dryness. The products were obtained by recrystallization from methanol–ether (yield: 92–96%). Gelator **1**–**2**: a pyridine solution (100 mL) of halogen compound (20 mmol) was heated at 100 °C for 12 h under a nitrogen atmosphere. The resulting solution was evaporated to dryness. The product was obtained by recrystallization from methanol–ether (yield: 96%). Counter anion exchange reaction from Br^- to SO_4^{2-} and PO_4^{3-}: to an aqueous solution of **1b** (30 mmol/300 mL), ammonium sulfate (15 mmol/20 mL), or sodium phosphate (10 mmol/20 mL) were added with stirring, and then the white precipitate was filtered and washed with water. The products were obtained by recrystallization from methanol–ether (yield: 98% for SO_4^{2-} salt and 85% for PO_4^{3-} salt).

Keywords: Hydrogel; Organogel; Gelator; Amphiphile.

* Corresponding author. Tel.: +81 268215499; fax: +81 268215608; e-mail: msuzuki@giptc.shinshu-u.ac.jp

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Table 1. Hydrogelation properties of **1**–**2** in various aqueous solutions[a]

	H_2O[b]	Saline	0.1 M							1.0 M						
			HCl	H_2SO_4	H_3PO_4	AcOH	NaCl	$MgCl_2$	$CaCl_2$	HCl	H_2SO_4	H_3PO_4	AcOH	NaCl	$MgCl_2$	$CaCl_2$
1a	15	7	9	3	20	15	9	7	7	10	Ins	8	25	10	15	13
1b	20	9	7	2	20	27	6	8	7	5	Ins	4	25	25	26	25
2a	20	8	8	3	12	20	12	13	13	17	Ins	3	40	20	23	23
2b	30	21	8	3	15	25	10	10	10	20	Ins	5	16	12	7	7

[a] Values denote minimum gel concentration (MGC, g/L) necessary for hydrogelation and organogelation at 25 °C.

[b] Pure water. Ins: almost insoluble.

gelation properties of **1** and **2** in aqueous solutions are listed in Table 1. In pure water, these compounds formed a hydrogel, although their hydrogelation abilities were less than the L-lysine-based hydrogelators reported previously.[9b] For the aqueous solutions of acetic acid, the similar hydrogelation abilities were observed, indicating that the acetic acid hardly affected their hydrogelation abilities. In the presence of inorganic salts, their hydrogelation abilities significantly increased at the low concentration (0.1 M), while, at the high concentrations (1.0 M), the hydrogelation abilities decreased and were similar to those in pure water. Although the hydrogelation in aqueous HCl solutions showed almost the same behavior as inorganic salt systems, the results in aqueous H_2SO_4 and H_3PO_4 solutions were quite different. In 0.1 M H_2SO_4 solution, the best hydrogelation abilities were observed; **1** and **2** formed the hydrogels around 0.2 wt%. However, **1** and **2** were insoluble in 1.0 M H_2SO_4. In contrast, their hydrogelation abilities increased with the increasing concentration of H_3PO_4. These results indicate that the exchange of counter anions contributes to the hydrogelation. In order to evaluate the influence of counter anion, we synthesized the L-valine and L-isoleucine derivatives with SO_4^{2-} or PO_4^{3-} as a counter anion[†] and examined their hydrogelation abilities in pure water. As the results, the L-valine and L-isoleucine derivatives with SO_4^{2-} were water insoluble. In contrast, the L-valine and L-isoleucine derivatives with PO_4^{3-} could gel pure water around 1.5 wt%. From the elemental analyses, however, these were a mixture of the compounds with PO_4^{3-}, HPO_4^{2-}, and $H_2PO_4^{-}$; that is, complete anion exchange from Cl^- and Br^- to PO_4^{3-} did not occur. The facts suggest that the hydrogelation abilities increase by partial exchange of the counter anions, but not complete. Interestingly, these compounds also have organogelation abilities for some organic solvents. The L-valine derivatives, **1a** and **1b**, can gel cyclohexanone, cyclic ethers, aromatic solvents, DMSO, acetonitrile, and oils such as oleic acid and linoleic acid. Although the L-isoleucine derivatives, **2a** and **2b**, have less organogelation abilities than **1a** and **1b**, they gel cyclic ethers and oils. Therefore, L-valine and L-isoleucine derivatives are amphiphilic gelators with a positively charged terminal group, which can form not only organogels but also hydrogels (Table 2).

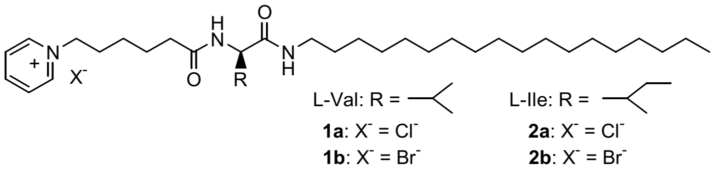
In the organogels and hydrogels, the gelator molecules often self-assemble into nano-scaled superstructures. Figure 1 shows the TEM photographs of samples prepared from the hydrogels and organogels based on **1a**. As expected, these gelators created a three dimensional network by entanglement of the self-assembled nanofibers in the hydrogels and organogels.

The gelation mechanism was investigated using an FT-IR spectroscopy. Figure 2 shows the FT-IR spectra of **1a** in $CHCl_3$ and CCl_4 gel. In the $CHCl_3$ solution (non-organogelation), the typical IR bands, arising from non-hydrogen bonded amide group, were observed at 3428 cm^{-1} (νN–H, amide A), 1657 cm^{-1} (νC=O, amide I), and 1523 cm^{-1} (δN–H, amide II). The FT-IR spectra of CCl_4 gel based on **1a** showed the IR bands at 3295 cm^{-1} (amide A), 1629 cm^{-1} (amide I), and 1543 cm^{-1} (amide II), characteristics of hydrogen bonded amide groups. In addition, the IR bands of the antisymmetric (ν_{as}) and symmetric (ν_s) CH_2 stretch-

Table 2. Organogelation properties of **1**–**2** in various solvents[a]

	1a	**1b**	**2a**	**2b**
H_2O–EtOH (1:1)	P	15	S	10
Cyclohexane	VS	VS	PG	VS
Cyclohexanone	12	16	12	VS
THF	8	11	19	30
1,4-Dioxane	9	4	25	30
Toluene	27	26	VS	VS
Chlorobenzene	4	7	VS	VS
Nitrobenzene	7	5	8	10
DMSO	24	VS	24	P
Acetonitrile	7	15	11	8
CCl_4	10	12	10	12
Oleic acid	20	15	15	15
Linoleic acid	15	15	15	15

[a] Values denote minimum gel concentration (MGC, g/L) necessary for hydrogelation and organogelation. VS: viscous fluid at 5 wt% (50 g/L). P: precipitate. PG: partial gel consisting of gel and solution.



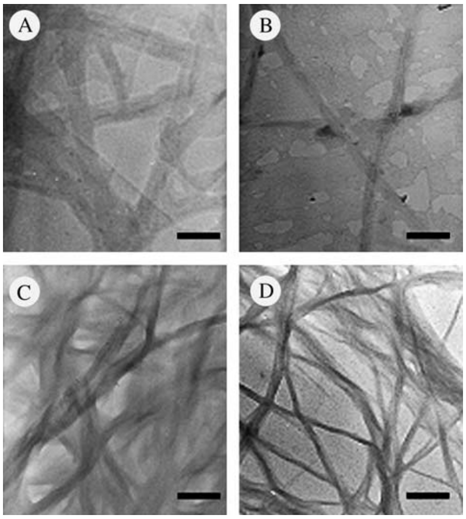


Figure 1. TEM photographs of dried gels prepared from hydrogels and organogels: (A): hydrogel based on **1a**; (B): 0.1 M NaCl hydrogel based on **1a**; (C): THF gel of **1a**; (D) cyclohexanone gel of **1a**. Scale bars are 200 nm.

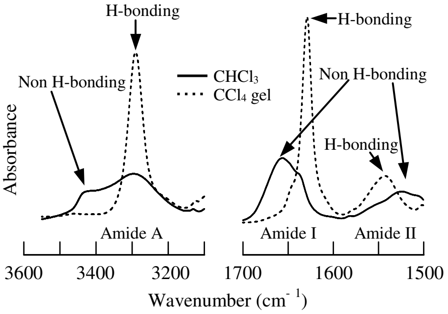


Figure 2. FT-IR spectra of **1a** in $CHCl_3$ solution (solid line) and CCl_4 gel (dashed line); [**1a**] = 20 mg/mL.

ing vibrations of **1a** in the CCl_4 gel shift to the lower wavelength compared with those in $CHCl_3$ [2927 cm^{-1} (ν_{as}, C–H) and 2855 cm^{-1} (ν_s, C–H)] and appeared at 2923 cm^{-1} (ν_{as}, C–H) and 2852 cm^{-1} (ν_s, C–H), which indicates that the alkyl chains of **1a** have a low fluidity.[11] These facts imply that the organogelation takes place through hydrogen bonding as a main force and van der Waals interaction as a complementary force.

Figure 3 shows the FT-IR spectra of **1a** in the D_2O gel (at 25 °C) and in D_2O solution (at 80 °C). In a hot D_2O solution, the IR spectrum showed the absorption bands at 1636 cm^{-1} and shoulder band around 1660 cm^{-1} in the amide I region, while two absorption bands were observed at 1640 and 1612 cm^{-1} in the D_2O gel obtained by cooling the hot solution. These bands arise from the intermolecular hydrogen bonded amide I. The absorption bands arising from the alkyl groups shifted from 2924 to 2916 cm^{-1} (ν_{as}, C–H) and from 2854 cm^{-1} and 2848 cm^{-1} (ν_s, C–H), indicating the strong hydrophobic interaction between the alkyl groups. Because these IR peaks of the alkyl groups appear at the lower wavelength than those in the organogel, the alkyl groups in the hydrogel undergo a stronger interaction. Therefore, the driving forces for the formation of a hydrogel are mainly hydrophobic interaction and complementarily hydrogen bonding.

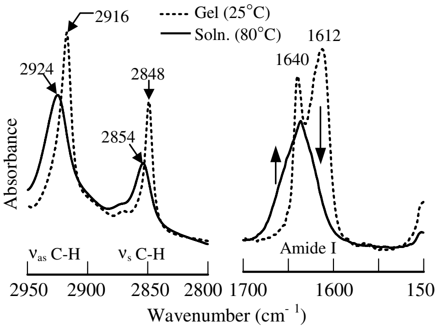


Figure 3. FT-IR spectra of **1a** in D_2O gel at 25 °C (dashed line) and D_2O solution at 80 °C (solid line); [**1a**] = 40 mg/mL.

In summary, we revealed the gelation properties of new low-molecular-weight gelators based on L-valine and L-isoleucine with a positively charged terminal. These compounds function as an amphiphilic gelator that can form not only supramolecular hydrogels in pure water, saline, and aqueous solutions containing inorganic salts and acids but also organogels in some organic solvents and oils. The FT-IR studies demonstrate that the main driving force is hydrogen bonding between the amide groups for organogelation and hydrophobic interaction for hydrogelation.

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