doi:10.1246/cl.2011.1143
Published on the web September 23, 2011

Cyclo(L-aspartyl-L-phenylalanyl)-containing Poly(dimethylsiloxane)-based Thixotropic Organogels

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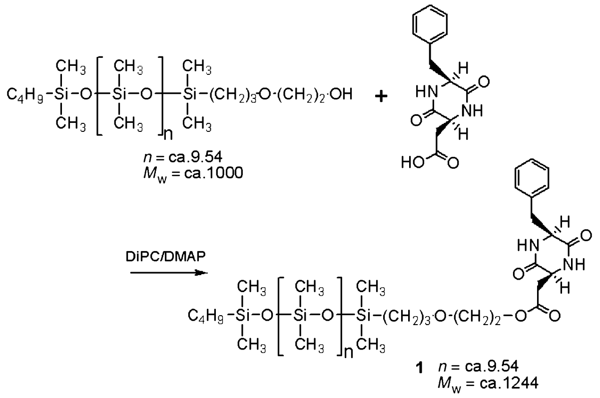
Cyclo(L-aspartyl-L-phenylalanyl)-containing poly(dimethylsiloxane) was synthesized through a simple procedure. This compound had a good organogelation or thickener ability in many organic solvents. X-ray diffraction showed that the gelator forms amorphous structure due to the presence of poly(dimethylsiloxane). Furthermore, some organogels were thixotropic in that reversible gel-to-sol transition was induced by mechanical stress.

Low-molecular-weight gelators (LMWGs) have attracted much interest because of their potential applications.[1–3] The LMWGs based on amino acids have good gelation ability in various solvents,[4] since gelation occurs as a result of cooperating noncovalent forces, such as hydrogen-bonding, van der Waals, π–π stacking, coordination, and electrostatic interactions. On the other hand, many polymer organogelators have been reported, where LMWGs are introduced into conventional polymers, such as polypeptides,[5] polycaprolactone,[6] poly(propylene glycol),[7] poly(ethylene glycol),[8] and others.[9] These gelators showed good gelation ability in various organic solvents. Introducing conventional polymer into a LMWG is an important strategy for development of new gelators. Therefore, we focused our attention on the kind of polymer material. Herein, poly(dimethylsiloxane) (PDMS) was chosen as a material to develop new gelators. PDMSs have been applied to commercial products, such as foods, cosmetics, health care products, textiles, construction materials, electronics, and industrial chemicals.[10] PDMSs and their derivatives are produced as useful commercially available products. In this paper, we describe the synthesis of a new gelator that consists of commercially available PDMS and cyclo(L-aspartyl-L-phenylalanyl) as the LMWG driving force.

Cyclo(L-aspartyl-L-phenylalanyl) was easily obtained from *N*-L-α-aspartyl-L-phenylalanine 1-methyl ester (Aspartame), a well-known artificial sweetener.[11] **1** was synthesized by the coupling reaction of cyclo(L-aspartyl-L-phenylalanyl) and commercially available poly(dimethylsiloxane) (M_w = ca. 1000) as shown in Scheme 1, and identified by FT-IR, ^{1}H NMR, and GPC (see Supporting Information[16]).

The gelation behavior of **1** is listed in Table 1, where values mean minimum gel concentration (MGC) necessary to harden liquids at 25 °C. For comparison, the gelation behavior of cyclo(L-*O*-dodecylaspartyl-L-phenylalanyl) is shown in the same table. The MGC values were determined by inverse test tube. **1** is a good gelator for hydrocarbons and oils and forms transparent gels. Additionally, gel prepared from **1** was thixotropic.[12,13] The formed gel was stable even after a few years. It is noteworthy that **1** forms organogels in liquid paraffin, isopropyl myristate, D-4, and D-5, which are often used as solvents for cosmetics. In contrast, although **1** showed no gelation in *n*-hexane and cyclohexane, **1** functioned as a thickener in those solvents, e.g., the viscosity of cyclohexane containing **1** (2 wt %) was more than 1000 times higher than that of cyclohexane.



Scheme 1. Synthetic procedure for **1**.

Table 1. Gelation by **1**[a]

Liquids	Aspects and MGC	
	1	cyclo(L-*O*-dodecyl aspartyl-L-phenylalanyl)
Hexane	Viscous fluid	Insoluble
Cyclohexane	Viscous fluid	Insoluble
Decane	Thixotropic gel (25)[b]	Insoluble
Liquid paraffin	Thixotropic gel (5)[b]	Insoluble
Toluene	Thixotropic gel (20)[b]	Insoluble
Xylene	Thixotropic gel (20)[b]	GO[c]
1,3,5-Trimethylbenzene	Thixotropic gel (10)[b]	GO[c]
Isopropyl myristate	Thixotropic gel (5)[b]	GO[c]
D-4	Thixotropic gel (20)[b]	Insoluble
D-5	Thixotropic gel (20)[b]	Insoluble
Methanol	Soluble	GO[c]
Ethanol	Soluble	GO[c]
Water	Insoluble	Insoluble

[a]Values mean MGC at 25 °C; the unit is g L^{-1} (gelator **1**/liquid). D-4: octamethylcyclotetrasiloxane, D-5: decamethylcyclopentasiloxane. [b]Thixotropic behavior was briefly checked when sample was agitated after 30 min in test tube. [c]GO means opaque gel. The sample transformed into a precipitate after several days.[11]

The temperature-controlled FT-IR spectra of **1** in decane showed that the hydrogen-bonding interaction was one of the driving forces for the gelation (Figure S1[16]). The spectrum of gel at 55 °C showed an absorption at 1671 cm^{-1} assigned to the hydrogen-bonded amide I (ν C=O). The peak at 1671 cm^{-1} gradually shifted to 1701 cm^{-1} is assigned to non-hydrogen-

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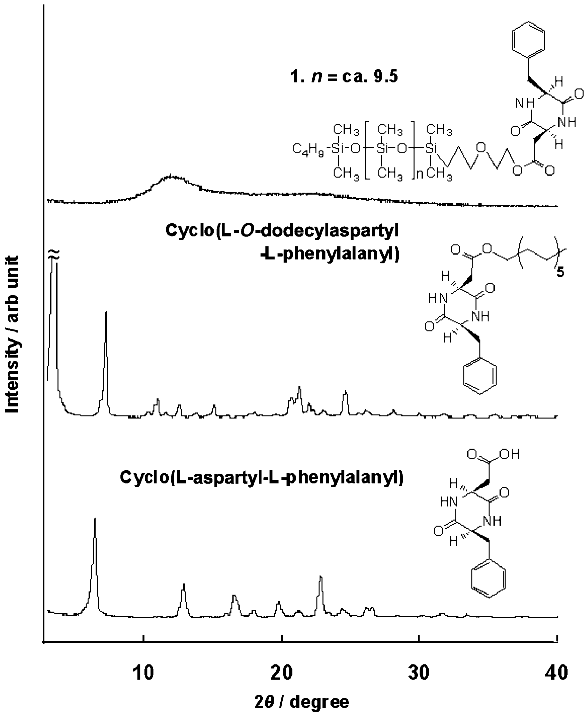

Figure 1. PXRD patterns of cyclo(L-aspartyl-L-phenylalanyl), cyclo(L-*O*-dodecylaspartyl-L-phenylalanyl), and compound **1**.

bonding stretching vibration with increasing temperature. These results led us to conclude that hydrogen bondings among amides are formed in gel state and the transition into solution with increasing temperature is attributable to the disintegration of hydrogen bondings.[1]

In addition, the TEM image of the dried gel prepared from toluene gel of **1** showed a three-dimensional network formed by self-assembled nanofibers (Figure S2[16]). The self-assembled nanofibers were often observed in samples which were prepared from the amino acid gelators.[1,2d,4,11]

Figure 1 shows the XRD patterns of **1**, cyclo(L-aspartyl-L-phenylalanyl), and cyclo(L-*O*-dodecylaspartyl-L-phenylalanyl), where cyclo(L-aspartyl-L-phenylalanyl) is the precursor of **1**, and cyclo(L-*O*-dodecylaspartyl-L-phenylalanyl) is synthesized from cyclo(L-aspartyl-L-phenylalanyl) and dodecyl alcohol.[11] The XRD analyses of cyclo(L-aspartyl-L-phenylalanyl) and cyclo(L-*O*-dodecylaspartyl-L-phenylalanyl) exhibited many sharp diffraction peaks as a result of its crystalline structure. In contrast, the XRD profile of **1** showed broad peaks, indicating that **1** was amorphous. This suggests that the PDMS segment inhibits the crystallization of cyclo(dipeptide) segments. As reported previously, cyclo(L-aspartyl-L-phenylalanyl) has a very low solubility in many solvents due to its strong intermolecular interactions in the crystalline state, while cyclo(L-*O*-dodecylaspartyl-L-phenylalanyl) is soluble in few solvents and has gelation ability in few solvents.[11] These facts imply that the introduction of PDMS, instead of linear alkyl groups, into the cyclo(L-aspartyl-L-phenylalanyl) improves the gelation ability. Very interestingly, the gels formed by **1** are thixotropic. Figure 2 shows the thixotropic behavior of decane gel of **1**.

Figure 2. Photographs of decane containing **1** ($30\,\mathrm{g\,L^{-1}}$). (A) Gel formed from hot solution on cooling process, (B) low-viscosity fluid formed by vigorous hand-shaking, and (C) gel reformed after left standing for a few minutes.

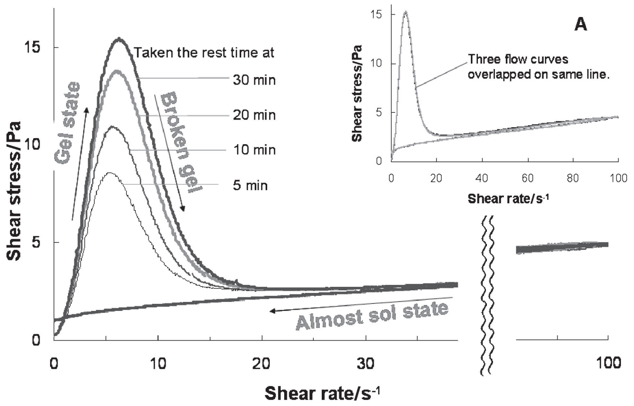

Figure 3. Hysteresis loop of decane gel of **1** ($20\,\mathrm{g\,L^{-1}}$) at 25 °C. The 4 curves were taken after the settled rest time (from top 30, 20, 10, and 5 min). Inset **A** shows three hysteresis loops carried out with 30 min standing time.

When the decane gel (photograph A) was vigorously shaken at 25 °C, the gel changed into sol (photograph B). After standing for a few minutes at 25 °C, the solution returned to the gel state again (photograph C). It is noteworthy that such thixotropic behavior can be repeatedly carried out at 25 °C. It is known that thixotropic behavior is a mixing system (e.g., colloidal suspension) where time-dependent, reversible breakdown of the particulate network structure occurs under shear, followed by structural reformation on resting.[12,14,15] The thixotropicity was studied using a rotational rheometer equipped with a double-cylinder fixture; the decane gel of **1** (2.0 wt/vol %) was kept at 25 °C for 2 h before measurement. To investigate the time-dependence of viscoelasticity of the samples, flow curves were measured after each rest time. Figure 3 shows the flow curves which were taken after a rest time of 30, 20, 10, and 5 min, respectively. Typical hysteresis loops were observed. The shear stress increased and them decreased via the maximum value with the increasing shear rates, while it linearly decreased with the decrease shear rates. In the case of precursor polymer, poly(dimethylsiloxane), such rheological behavior was not observed because the polymer does not show organogelation for any solvents. A peak of shear stress appeared involving the collapse of the gel, and the linear decrease of stress showed that the sample was almost sol.[12] Another measurement after 20 min of rest standing in a rheometer showed a smaller local peak than 30 min. Presumably, it happened due to the incomplete recovery of viscosity. Therefore, the local peaks decreased with decreasing rest time. Inset **A** shows three hysteresis loops carried out with 30 min standing time. These results were repeatedly and reproducibly seen within the same rest time, even if this measurement was performed many times at 25 °C. As a result, this sample shows a semipermanent sol–gel phase transition induced by shear stress at 25 °C.

To investigate the relationship between hydrogen bonding and thixotropic behavior, we acquired an FT-IR spectrum of the thixotropic gel. However, the peak at 1671 cm^{-1} was not changed by shear.

In conclusion, we revealed the simple synthesis of new organogelator **1** and its organogelation abilities. The compound functions as either a gelator or a thickener in many organic solvents. The XRD studies suggested that the PDMS segment inhibits the crystallization of cyclo(dipeptide) segment. Therefore, the gelation ability of cyclo(dipeptide) derivative was influenced by the polymer chain as stabilizing segment. It seemed that the amorphous structures have an effect on solubility, gelation ability, and viscoelasticity. The transparent gel prepared by **1** undergoes a reversible sol–gel phase transition not only by heating but also by shear stress. Namely, the gel is thixotropic.

This work was supported by a research fellowship of the Japan Society for the Promotion of Science for Young Scientists (to H.H) and Grant-in-Aid for Global COE Program by the Ministry of Education, Culture, Sports, Science and Technology.

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