Metal Ion-induced Chirality and Morphology Control of Self-assembling Organogels from L-Glutamic Acid-derived Lipids

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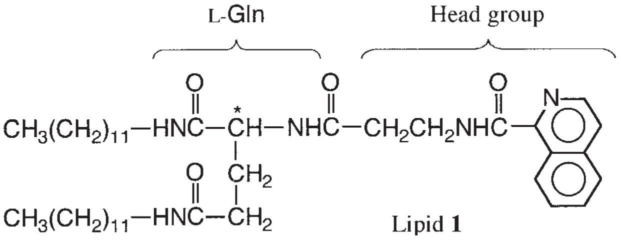
L-Glutamic acid-derived lipid with an isoquinolinyl head group formed nanofibrous aggregates based on highly-ordered structures in organic media. CD spectra and TEM observations indicated that the aggregation morphology and the chirality can be controlled by complexation with metal ions.

It is known that special synthetic lipids work as self-assembling organogelators.[1] These gelations have been often brought through network formation with well-developed fibrous aggregates of their lipids. In the last decade, many chiral synthetic lipids have been derived from peptides[2] or saccharides[3] for this purpose because intermolecular hydrogen bondings through their amide bondings and hydroxyl groups are very effective for self-assembling in organic solutions. Therefore, organogels open up as new chiral organic media although there have been a few reports.[4,5] As supporting this expectation, we have shown the first example of enantioselective elution from chiral organogels.[4] To expand possible application as chiral media, it should be very important to control the chirality. In this communication, we report that an L-glutamic acid-derived lipid **1** with a chelating head group was newly synthesized as a self-assembling organogelator and the chirality could be controlled by the chelation with a metal ion.



Lipid **1**

The chemical structure of **1**[6] was designed on the basis of the fact that the triamide structure from L-glutamide (L-Gln) promotes molecular orientation through hydrogen bondings. Typical examples have been realized as formation of nanofibrillar aggregates in aqueous[7–9] and organic[10,11] solution systems. In this study, an isoquinolinyl group was chosen as a chelating head group while some of researchers have adopted crown ethers[12,13] and saccharide derivatives.[14] However, an isoquinolinyl moiety gives us some advantages: for example, (1) the compact and planar structure does not interfere the molecular orientation among the lipids and (2) it is usable as a sensitive chromophoric group to evaluate physicochemical properties of the aggregates.

When the lipid **1** was dissolved in a hot organic solvent such as benzene, toluene, cyclohexane, a cyclohexane–ethanol (100 : 1) mixture and then the solution was allowed to stand at 10 °C, clear or slightly-turbid gels were produced. It was observed visually that the sol-to-gel transition in the cooling process occured at around 35–40 °C and 15–20 °C in benzene and a cyclohexane–ethanol (100 : 1) mixture, respectively. The DSC measurement showed that these thermally-induced sol-to-gel transitions were detected with exothermic peaks whose peak-top temperatures were located at 33 and 15°C, respectively.

The critical gelation concentration (cgc) was dependent on a kind of solvent and estimated by an inversion fluid method[15] to be between 1–2 mmol dm^{-3} and 0.5–1 mmol dm^{-3} benzene and a cyclohexane–ethanol (100 : 1) mixture, respectively. Well-developed fibrous aggregates were detected by TEM observations. This is probably a strong piece of evidence that the gelation is brought through fibrillar network formation. However, it should be mentioned that macroscopic measurements were not always helpful to understand microscopic aggregation states. For example, the value of cgc is absolutely dependent on the viscosity of solution and the interconnection density and strength of fibrillar aggregates. TEM observation also may not provide true aggregation morphology because the concentration process is necessarily included. Therefore, we adopted CD spectral measurement to evaluate the aggregation state. As a result, extremely enhanced CD spectra[16] were observed for the cyclohexane–ethanol (100 : 1) solution of **1** (0.3–0.03 mM, 5–20 °C) in 200–250 nm which is attributable to the absorption of the carbonyl groups. The CD enhancement was also observed in 250–350 nm which could be assigned by the isoquinolinyl group as shown in Figure 2. Similar enhancement and induction of chirality have been often reported in aqueous lipid membrane systems from chiral lipids and they are explained by formation of highly-ordered structures with chiral orientation.[17,18] Therefore, these results indicate that **1** can form highly-ordered structures in the dilute solution and that the critical aggregation concentration (cac) can be estimated by examining the concentration dependency on the molecular ellipticity. The cac's were determined by the bending point in the concentration-$[\theta]_{230}$ plots to be 0.3 mmol dm^{-3} and 0.03 mmol dm^{-3} at 10 °C in benzene and a cyclohexane–ethanol (100 : 1) mixture, respectively.

The significant purpose of this work is to control the chirality by chelating with metal ions. For this purpose, we focused on Cu^{2+} and Co^{2+} with different coordination structures. As shown in Figure 2, we observed that these metal ions induced unique stress to the **1** aggregates. The typical examples can be explained with their absorption and CD spectra and TEM observation as follows: the complexation with metal ions was estimated by detecting a λ_{max}-shift of the isoquinoline moiety. This was

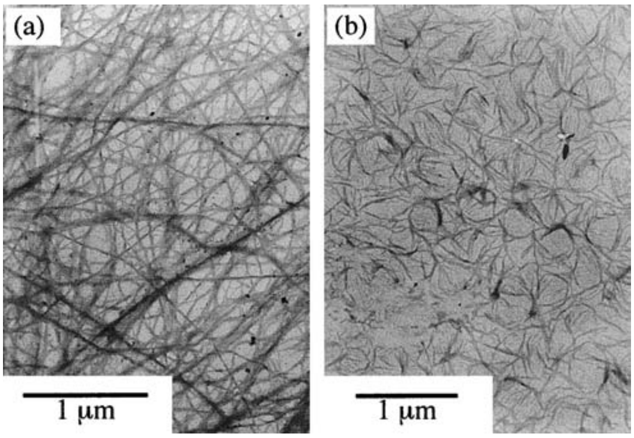


Figure 1. Typical TEM images of lipid **1** aggregates casted from cyclohexane–ethanol (100 : 1) solution (1 mmol dm^{-3}) in the absence (a) and in the presence (b) of Co^{2+} (0.5 mmol dm^{-3}).

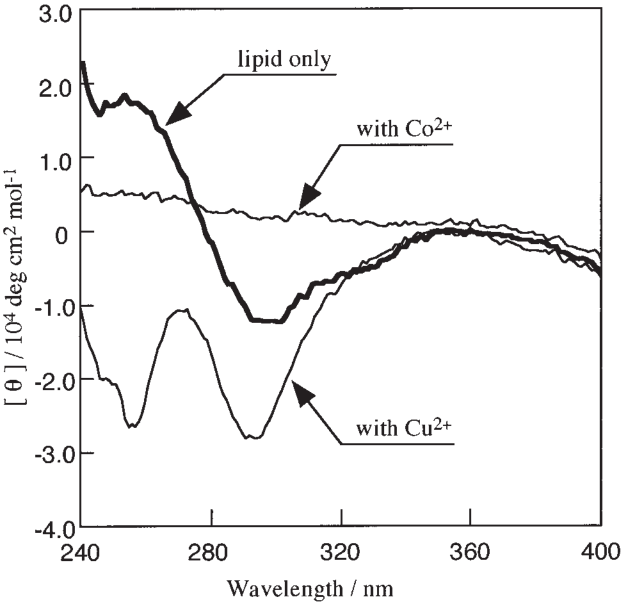


Figure 2. Circular dichroism spectra of **1**-aggregates with metal ions in cyclohexane–EtOH (100 : 1) mixture at 15 °C. [**1**] = 0.3 mmol dm^{-3}, [CuCl$_2$] and [CoCl$_2$] = 0.15 mmol dm^{-3}.

accompanied by drastic CD spectral change. As shown in Figure 2, the addition of an equimolar of Cu^{2+} induced a completely different CD pattern showing enhancement around 258 nm and 290 nm. This indicates that Cu^{2+} promotes to produce new chiral microenvironment. However, it was confirmed by TEM that Cu^{2+} had no serious damage on the aggregation morphology in this condition (Figure 1a). Similarities were observed in Be^{2+}. On the contrary, different action was observed in Co^{2+}. Co^{2+} reduced CD strength remarkably as shown in Figure 2. TEM observation showed that only fragmented fibrous aggregates were detected (Figure 1b). Similar reduction of the chirality and fragmentation of the aggregates were observed by Zn^{2+}.

The detailed structures of the complexes with **1** have not been specified yet. However, we can be fairly certain that the isoquinolinyl group plays an important role for responding to metal ions. This can be supported by additional experiments: there was no significant change in CD spectra and TEM observations regardless of a kind of metal ion when an isoquinolinyl group was replaced by a benzyloxycarbonyl group. Here, we estimate that, if Cu^{2+} works to form a square planar coordination structure, the chelation with **1** does not interfere to maintain the highly-oriented structure. However, if Co^{2+} works to form an octahedral coordination structure, it is not profitable to keep their original highly-oriented structures.

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6 Lipid **1**: mp. 168–170 °C. Calcd for C$_{42}$H$_{69}$N$_5$O$_4$: C, 71.2; H, 9.82; N, 9.89%. Found: C, 70.9; H, 9.79; N, 9.50%.

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15 The inverse fluid method was carried out using a ϕ 14 mm sample tube at each temperature.

16 $[\theta]_{230}$ was 2.2×10^5 deg cm^2 dmol^{-1} at 10 °C and -1.5×10^4 deg cm^2 dmol^{-1} at 50 °C in the cyclohexane–ethanol (100 : 1) solution containing 0.3 mM of **1**.

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