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Novel self-assembling organogelators by combination of a double chain-alkylated L-glutamide and a polymeric head group †

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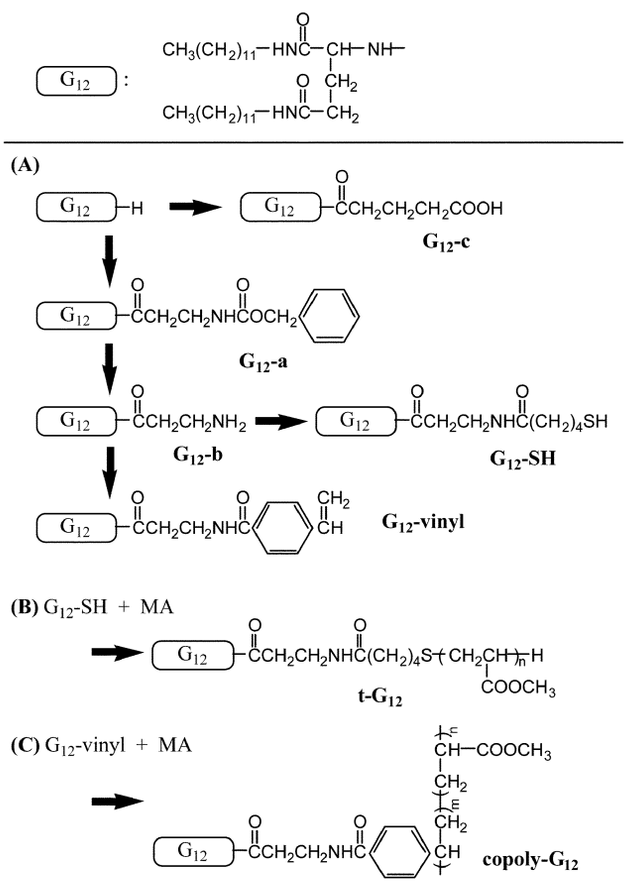
This communication introduces a new class of self-assembling organogelators composed of a double chain-alkylated L-glutamide with a polymeric head group.

Since reports in the late 1980s to early 1990s that some lipophilic low molecular weight compounds such as cholesteryl and peptide-containing derivatives could produce self-assembled organogels,[1–5] they have been expected to play a role as novel organic media for nano-devices and for chemical reaction and separation. In the past half decade, there have been many reports on theoretical and physicochemical as well as experimental research.[6–9] One attractive feature of organogels is their specific chirality[10–13] as most organogelators possess molecular chirality which works as a driving force for nanofibrillar aggregate formation. Additional functionalization of organogels has often been done by direct introduction of functional groups into organogelators. Typical examples are crown ether-,[3,12,15] azobenzene-,[3,4,14] pyrene-,[15] spiropyran-,[16] naphthopyran-,[17] porphirine-,[15,18] isoquinoline-[11] and polymerizable unit-containing[19–21] derivatives. Such chemical modifications serve to expand their possible applications. Here, we introduce a new approach to making functional organogelators based on the fact that additional functionalities can be introduced by polymerization, which will facilitate the introduction of versatility into a molecule. In this communication, we report a preliminary example of poly(methyl acrylate) derivatives newly-synthesized for this purpose that can form self-assembled organogels in several organic solvents through highly-oriented aggregate formation.

Scheme 1 summarizes the synthetic procedure for poly(methyl acrylate) derivatives containing the double-chain alkylated L-glutamide ($\mathbf{G_{12}}$). In this scheme, the $\mathbf{G_{12}}$ moiety is very important as a key unit to create highly-oriented nanofibrillar aggregates in either or both aqueous[10] and organic[4,8,10] solution systems. For example, $\mathbf{G_{12}}$-**b**[22] and its related amphiphilic compounds[23,24] can form nanotubular and/or nanohelical aggregates on the basis of bilayer membrane structures in their dilute aqueous solutions. On the other hand, lipophilic $\mathbf{G_{12}}$-**a** was dissolved at 0.3 wt% in hot benzene to make clear gels at room temperature.[4] $\mathbf{G_{12}}$-**c** can form nanofibrillar aggregates both in aqueous and organic solution systems.[24] Three amide bondings of the $\mathbf{G_{12}}$ unit are in a favorable position for intermolecular interaction among lipids to promote the formation of highly-oriented structures, even if a sterically bulky head group is not chosen.



Scheme 1 Chemical structures of organogelators derived from double-chain alkyl L-glutamide ($\mathbf{G_{12}}$).

The polymer, $\mathbf{t\text{-}G_{12}}$ was prepared by a one-step radical telomerization of methyl acrylate (**MA**) initiated with the ω-mercaptoalkylated $\mathbf{G_{12}}$ ($\mathbf{G_{12}}$-**SH**).‡ The average degree of polymerization (n) was controlled by adjusting the ratio of $\mathbf{G_{12}}$-**SH** to **MA**. We obtained two kinds of $\mathbf{t\text{-}G_{12}}$ with n values of 10 and 25.‡ The copolymer (copoly-$\mathbf{G_{12}}$) was prepared by copolymerization of $\mathbf{G_{12}}$-vinyl with **MA**. The composition (n/m) could be controlled by adjusting the initial molar ratio of $\mathbf{G_{12}}$-vinyl to **MA**. The resultant compositions were 2, 4 and 12.‡

It was confirmed that both $\mathbf{t\text{-}G_{12}}$ and copoly-$\mathbf{G_{12}}$ could easily dissolve in hot benzene and then produce clear organogels when kept at room temperature. Similar gelation behaviors were

† Electronic supplementary information (ESI) available: table of gel-to-sol transition temperatures for $\mathbf{G_{12}}$-containing polymers; SEM of a xerogel from copoly-$\mathbf{G_{12}}$; temperature dependence of CD spectra of $\mathbf{G_{12}}$-vinyl and copoly-$\mathbf{G_{12}}$; experimental and characterisation data for $\mathbf{G_{12}}$-**a**, $\mathbf{G_{12}}$-**b**, $\mathbf{G_{12}}$-vinyl and copoly-$\mathbf{G_{12}}$. See http://www.rsc.org/suppdata/ob/b3/b305928f/

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Table 1 Gelation properties of copoly-$\mathbf{G_{12}}$ at 25 °C

Solvents	*n*/*m*	Organogelators (wt%) 3.0	2.0	1.0	0.5	0.1
Benzene	$\mathbf{G_{12}}$-vinyl	Gel	Gel	Gel	Gel	Gel
	2	Gel	Gel	Gel	Gel	Sol
	4	Gel	Gel	Gel	Sol	Sol
	12	Gel	Gel	Sol	Sol	Sol
Cyclohexane–ethanol (9 : 1) mixture	$\mathbf{G_{12}}$-vinyl	Gel	Gel	Gel	Gel	Sol
	2	Gel	Gel	Gel	Gel	Sol
	4	Gel	Gel	Gel	Sol	Sol
	12	Sol	Sol	Sol	Sol	Sol

Gelation was observed by an inverse fluid method.

observed in toluene, cyclohexane and cyclohexane–ethanol mixtures, although slightly turbid gels were obtained in cyclohexane alone. The gelation properties of copoly-$\mathbf{G_{12}}$ were investigated in detail. As shown in Table 1, $\mathbf{G_{12}}$-vinyl can make a gel at a concentration of 0.1 wt% in benzene. The critical gelation concentration ‡ (cgc) is considerably lower than that of $\mathbf{G_{12}}$**-a**. This may be attributed to a side effect due to introduction of a polymerizable head group. Copolymerization with **MA** disturbed gelation ability slightly, but the cgcs in each **MA** content were observed at the reasonable concentrations of <0.5, <1.0 and <2.0 wt% in benzene and <1.0, <1.0 and <2.0 wt% in a cyclohexane–ethanol (9 : 1) mixture. As discussed below, the decrease in gelation ability with increasing **MA** content is related to the fact that fibrillar aggregates form on the basis of molecular orientation among the $\mathbf{G_{12}}$ moieties, which is influenced by the **MA** moieties.

It is known that freeze-drying methods convert organogels into xerogels which are useful materials for investigating gelation mechanisms.[8] Fig. 1 shows typical SEM images of the xerogels of copoly-$\mathbf{G_{12}}$ prepared from their benzene gels. It is clear that $\mathbf{G_{12}}$-vinyl produces a fibrillar network whose observed minimum diameters are about 40 nm. This is much larger than the molecular length[8] of the key unit ($\mathbf{G_{12}}$) of about 3 nm and thus allows us to imagine that the fibrils are made up of multi-wall layers or multi-strands. Supporting this assumption, thinner fibrils of 10 nm or so were detected by TEM observation. Similar fibrillar network formation has been widely detected with self-assembling organogelators;[6–9] thus we conclude that the gelation is brought about through formation of aggregate networks. On the other hand, copoly-$\mathbf{G_{12}}$ (*n*/*m* = 4 and 12) creates porous structures like multi-cellular structures while copoly-$\mathbf{G_{12}}$ (*n*/*m* = 2) shows fibrillar aggregates similar to those of $\mathbf{G_{12}}$-vinyl. Especially, copoly-$\mathbf{G_{12}}$ (*n*/*m* = 4) provides beautiful honeycomb structures. The average diameter of each cell is about 4 μm, which is much larger than the dense network with the $\mathbf{G_{12}}$-vinyl fibrils. It seems that the polymeric moiety of copoly-$\mathbf{G_{12}}$ promotes the production of layer-like structures rather than fibrillar structures.

The aggregation states of $\mathbf{G_{12}}$-derived molecules can be estimated by CD spectroscopy because of their molecular chirality. Fig. 2 shows typical CD spectra of organogels with $\mathbf{G_{12}}$-vinyl and copoly-$\mathbf{G_{12}}$ at 15 °C. A mixture of cyclohexane–ethanol (9 : 1) was used as a solvent to avoid strong absorption at 250 nm due to benzene. $\mathbf{G_{12}}$-vinyl provided a Davydov splitting around 260 nm with $[\theta]_{max} = \pm 0.8 \times 10^4$ deg cm^2 dmol^{-1} at 248 and 272 nm. This absorption band almost agrees with that of the vinyl benzoyl group as a polymerizable moiety. On the other hand, the gel state was not observed at 60 °C due to a sol state ‡ and then the cotton effects almost disappeared ($[\theta]_{max}$, within $\pm 0.05 \times 10^4$ deg cm^2 dmol^{-1}). Induction of chirality to achiral dyes has been explained by dipole–dipole interaction through formation of highly-oriented aggregates such as bilayer

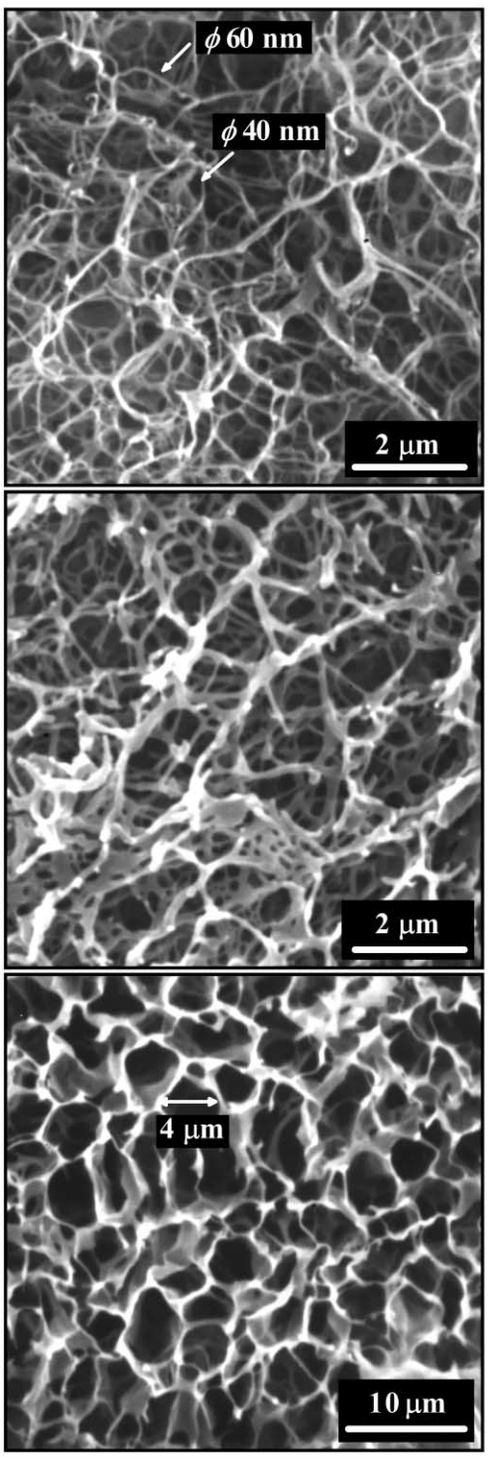

Fig. 1 SEM images of xerogels obtained from $\mathbf{G_{12}}$-vinyl (upper photo) and copoly-$\mathbf{G_{12}}$ (middle photo: *n*/*m* = 2; lower photo: *n*/*m* = 4) benzene gels. Initial concentrations are 1 wt%.

membrane systems with chiral lipids[11,22,25,26] and in complex formation on secondary structural polypeptides.[27,28] Therefore we may assume that the CD pattern at 15 °C is induced by chirally-stacked orientation among the polymerizable groups but the thermal gel-to-sol transition includes a remarkable decrease of molecular orientation.

As shown in Fig. 2, copolymerization of $\mathbf{G_{12}}$-vinyl with **MA** induced new CD bands both at 245 and 215 nm which belonged to the absorptions of the benzoyl and amide carbonyl groups, respectively. This indicates that the polymerization promoted chiral orientation around their groups through aggregation because their monomeric states provide much smaller CD strength. On the other hand, the polymerization was accom-

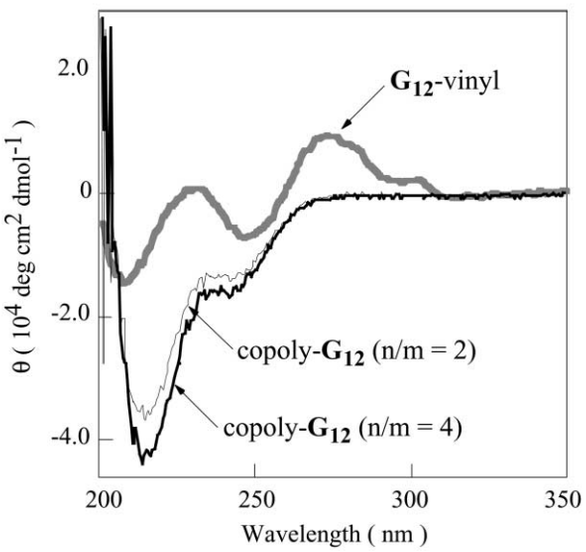

Fig. 2 CD spectra of a cyclohexane–ethanol (9 : 1) gels with $\mathbf{G_{12}}$-vinyl (5 mM) and copoly-$\mathbf{G_{12}}$ (5 unit-mM) at 15 °C. Copoly-$\mathbf{G_{12}}$ (n/m = 12) gel provides a similar CD specrum to that of copoly-$\mathbf{G_{12}}$ (n/m = 4).

panied by disappearance of the cotton effect around 260 nm indicating disappearance of the vinyl group.

When a cyclohexane–ethanol (9 : 1) gel with copoly-$\mathbf{G_{12}}$ was heated from 15 to 60 °C, the gel state collapsed into a sol state similarly observed in $\mathbf{G_{12}}$-vinyl.‡ However, the CD pattern was maintained even at 60 °C while the strength reduced to about 70%. These results indicate that highly-oriented aggregates with chiral order exist even in a sol state, but the aggregates are not well-developed to maintain a gel-formation network.

In conclusion, we have prepared a new class of L-glutamide-derived organogelators with polymeric groups and a molecular design which facilitates the addition of specific functionality. The copolymerization of a key unit with **MA** disturbs their gelation ability slightly, but the resultant gels include unique multi-cellular structures and the molecular orientation in the aggregates is more stabilized than the original organogelators. We expect this new class to expand possible applications of organogelators.

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Notes and references

‡ **$\mathbf{G_{12}}$-H**, **$\mathbf{G_{12}}$-a** and **$\mathbf{G_{12}}$-b** were obtained by previously reported methods.[8,11,22] **$\mathbf{G_{12}}$-H**: mp 118 °C. Anal. calc. for $C_{29}H_{59}N_3O_2$: C, 72.3; H, 12.3; N, 8.7. Found: C, 72.3; H, 12.4; N, 8.7%. **$\mathbf{G_{12}}$-a**: mp 178 °C. Anal. calc. for $C_{40}H_{70}N_4O_6$: C, 69.9; H, 10.3; N, 8.2. Found: C, 69.6; H, 10.2; N, 7.9%. **$\mathbf{G_{12}}$-b**: mp 144 °C. Anal. calc. for $C_{32}H_{64}N_4O_3$: C, 69.5; H, 11.7; N, 10.1. Found: C, 68.4; H, 11.4; N, 9.5%. **$\mathbf{G_{12}}$-SH** was derived from **$\mathbf{G_{12}}$-b** by coupling with γ-thiobutyrolactone: mp 218 °C. Anal. calc. for $C_{36}H_{70}N_4O_4S$: C, 60.0; H, 10.8; N, 8.6. Found: C, 64.3; H, 10.5; N, 8.2%. $\mathbf{G_{12}}$-vinyl was derived from **$\mathbf{G_{12}}$-b** by coupling with vinyl benzoyl chloride: mp 199 °C. Anal. calc. for $C_{39}H_{70}N_4O_4$: C, 72.0; H, 10.5; N, 8.2. Found: C, 72.0; H, 10.3; N, 8.0%.

The telomerization and polymerization were carried out in tetrahydrofuran, initiated with AIBN. The resultant telomers (**t-$\mathbf{G_{12}}$**) and copolymers (copoly-$\mathbf{G_{12}}$) were obtained from addition of methanol. ^{1}H-NMR did not show any proton signal belonging to a vinyl group. The average degree of polymerisation was determined by ^{1}H-NMR spectroscopy (400 MHz, $CDCl_3$) with the proton ratios at the chiral center of $\mathbf{G_{12}}$ (δ 4.35, s, CH) and the methoxy group of **MA** (δ 3.65, s, OCH_3).

The critical gelation concentration (cgc) was estimated by an inverse fluid method which was carried out using a ϕ 14 mm sample tube. The gel-to-sol transition temperature was also estimated by an inverse fluid method to be 53, 37, 32, 30, 41 and 39 °C in $\mathbf{G_{12}}$-vinyl, copoly-$\mathbf{G_{12}}$ (n/m = 2), copoly-$\mathbf{G_{12}}$ (n/m = 4), copoly-$\mathbf{G_{12}}$ (n/m = 12), **t-$\mathbf{G_{12}}$** (n = 10) and **t-$\mathbf{G_{12}}$** (n = 25), respectively.

Transmission and scanning electron microscopic (TEM and SEM) observations were carried out with JEOL JEM-2000FX and JSM-8310LV, respectively. Circular dichloism (CD) spectroscopy was carried out with JASCO J-725.

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