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Control of Macroscopic Helicity by Using the Sergeants-and-Soldiers Principle in Organogels

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Helical structures of biomolecules (e.g., proteins, nucleic acids) play a significant role in many natural systems. Because self-assembly is a powerful tool for constructing various types of nano- and microstructures, many artificial helices have been constructed for mimicking natural helical structures using self-assembly via hydrogen bonding, aromatic stacking and/or metal–ligand coordination interactions.[1] Since Green and co-workers set up a system based on the "majority" rule and the "sergeants-and-soldiers" principle,[2] various induced helical structures have been developed using Green's methods.[3] It turned out that the formation of homochiral helical structures only requires either the addition of a small portion of chiral units (sergeants) to the achiral units (soldiers) or having a slight majority of *R* over *S* units (or vice versa) in the supramolecules, because noncovalent interactions between chiral and achiral units can lead to chiral supramolecular structures by co-assembly of achiral and chiral monomers.

Recently, while considerable attention has been paid to the development of a low-molecular-weight gelator (LMWG) for use in organic solvents, there are more and more reports on nano- and microstructures being developed in the gelation process.[4] One of the structures of interest is a helical structure.[5] Although the control or amplification of chirality in gels becomes a matter of primary concern,[6] complete control of macroscopic helicity has never been reported in the gelation process (Figure 1.).

This is the first paper that reports on the control of macroscopic helical structures, which are self-assembled via hydrogen bonding, aromatic stacking, and van der Waals interactions between chiral and achiral organogelators, as well as on the unidirectional helicity of gels which are induced by the chiral organogelators. Although most sergeants-and-soldiers systems consist of chiral and achiral units that are structurally almost the identical, we exploit chiral and achiral units with different structures (see below). The achiral gelator **1** consists of a central aromatic group for aromatic stacking and alkylamide groups that can participate in intermolecular hydrogen bonds and van der Waals interactions. The chiral gelators **2** and **3** have alanine residues between the dodecanoyl and *p*-phenylenediamine groups as the chiral trigger unit. The gelators were synthesized by simple amide coupling in moderate yields (see Supporting Information).

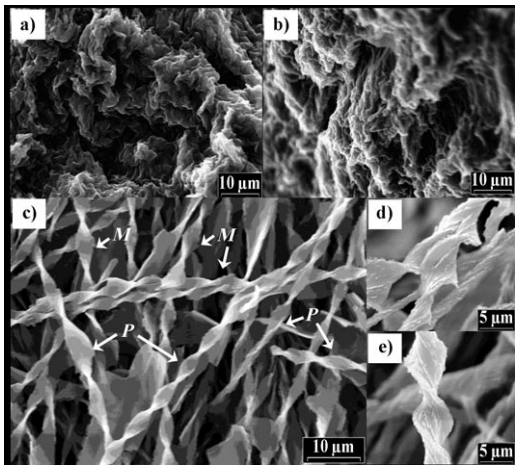

Figure 1. SEM images of xerogels, a) chiral gelator **2**, b) chiral gelator **3**, c) achiral organogelator **1**, d) and e) enlarged images of each *P* and *M* helix of **1** (scale bar: a)–c) = 10 μm, d) and e) = 5 μm).

NMR experiments were performed to obtain the evidence for π–π interaction and hydrogen-bonding interaction in organogelator **1**. The solvent polarity was varied by changing the methanol and chloroform composition (Figure 2a). NMR spectroscopy showed that the aromatic protons of organogelator **1** shifted upfield ($\delta = -0.95$ ppm) with increasing methanol ratio. These phenomena were attributed to an increase in the population of the π–π stacked, oligomeric or

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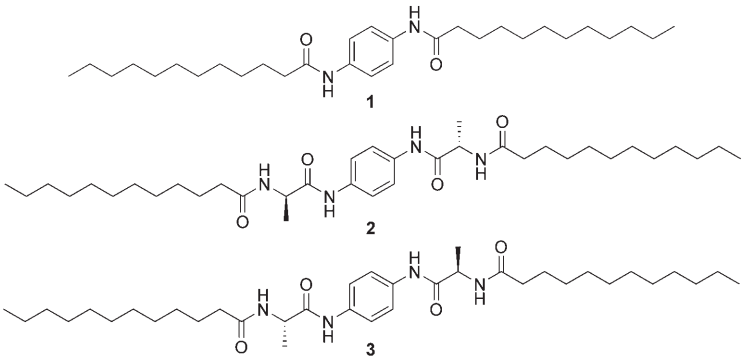

polymeric structures of organogelator **1**. This implies that the π–π interaction in organogelator **1** exerted a strong influence on self-association and gelation. The ^{1}H NMR signals of **1** are concentration-dependent in [D_8]toluene (Figure 2b). The amide proton signal shifted downfield ($\delta = +0.15$ ppm) upon increasing the concentration, whereas the aromatic proton signals showed insignificant shift. This indicated that hydrogen bonding is a crucial factor of self-association rather than aromatic stacking in toluene.

The gelation behavior of the gelators was tested in various organic solvents. Gelation occurred in aromatic solvents such as toluene and *p*-xylene. The xerogel obtained from achiral organogelator **1** in toluene (1.14% w/w) shows very interesting features in which remarkably thick ribbon structures are twisted in both left- and right-handed helical structures (Figure 1c, d and e). The width of the ribbons varies from 4 to 5 μm and they are a few hundred micrometers in length, with an average helical pitch length of 7–8.5 μm. The aggregated structures were stabilized presumably by cooperative aromatic stacking, hydrogen bonding, and van der Waals interactions. While aromatic stacking between the phenyl groups induces one-dimensional aggregates, hydrogen bonds among the amide groups propagate along the aggregate axis and enforce a helical mode of the aggregate.

For the purpose of controlling *P* and *M* helicity, chiral triggers **2** and **3** were used. It turned out that the chiral methyl group of the D- or L-alanine residue in **2** and **3** induced the formation of homochiral helical structures in the aggregates consisting of the achiral gelator and chiral gelator. Gelators **2** and **3** also formed organogels in toluene, but no helical fibers were observed when only a chiral gelator was present (Figure 1a, b). Various ratios (1:1, 2:1, 5:1, 10:1, 97:3, 98:2, and 99:1) of the achiral and chiral gelators were tested. When the chiral portion increased too much, the amount of the helical structure was not clear (Figure 3). Because the chiral methyl groups of **2** and **3** presumably inhibit the stacking interactions, an excess of either **2** or **3** probably obstructs the formation of helical structures. When the amount of **2** or **3** is above 33%, helical structures are clearly not formed (see Supporting Information).

The SEM images of xerogels exhibited the macroscopic aggregation modes of the gelators. Figure 4 shows that the xerogels obtained from complexes consist mainly of helical structures. Figure 4a and b shows that all helices formed by **1** and **2**, in the ratio of 99:1, reveal the characteristic left-handed helical ribbon structures (*M* helices). In the case of **1** and **3**, right-handed helical ribbon structures (*P* helices) are exclusively formed (Figure 4c and d). Because the width, length and average helical pitch length of helices are similar to those of the helices formed by **1** alone, chiral triggers **2** and **3** did nothing but play a role in inducing the unidirectional helicity.

CD experiments were performed to investigate the self-assembly of **1** and chiral triggers from a microscopic viewpoint. Gelator **1** was almost CD-inactive because organogels were constructed by the random placement of nearly equal numbers of *P* and *M* helices. In contrast, **2** and **3** show complementary CD spectra because of the presence of the in-

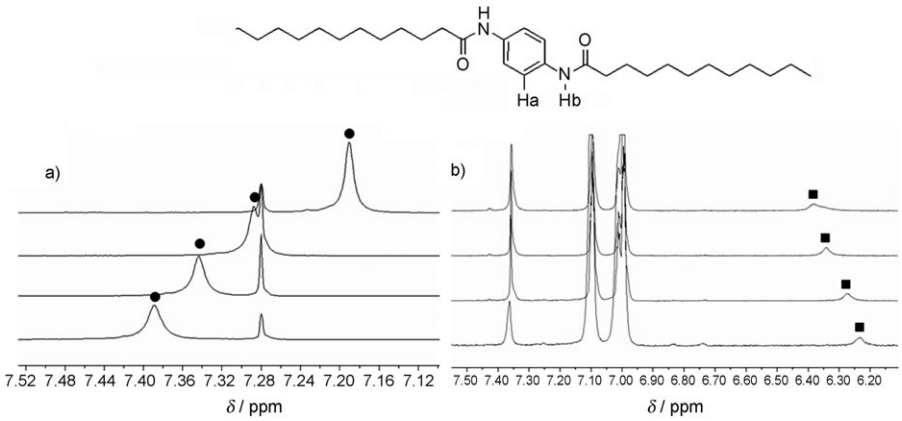

Figure 2. a) Stacked ^{1}H NMR spectra of 17 mM achiral gelator **1** at 50°C. The solvent ratio of $CDCl_3/CD_3OD$ (v/v) from bottom to top: 10:1; 5:1; 2:1; 1:1. b) Stacked ^{1}H NMR spectra of **1** are concentration-dependent in [D_8]toluene at 80°C. The concentration of **1** from bottom to top: 2, 4, 10, 20 mM. (H_a = ●, H_b = ■).

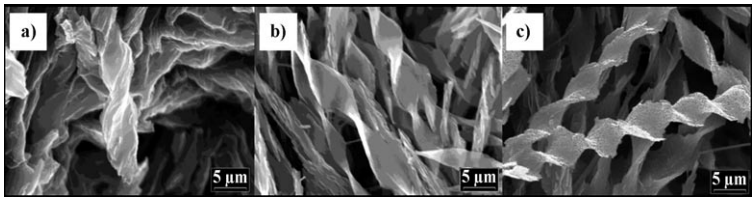

Figure 3. SEM images of xerogels a) **1/3** 1:1, b) **1/3** 10:1 and c) **1/3** 98:2 (scale bar a)–c) = 5 μm).

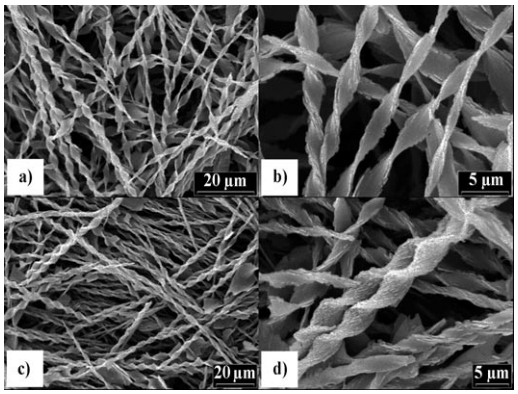

Figure 4. SEM images of xerogels a) and b) **1/2** 99:1, *M* helices, c) and d) **1/3** 99:1, *P* helices (scale bar a), c) = 20 μm and b), d) = 5 μm).

trinsic chirality in enantiomeric **2** and **3**. The fascinating fact is that assembly with only 1% of **2** or **3** provides a driving force for the complete induction of homochiral helices. As shown in Figure 5, addition of 1% of **2** induces the first positive Cotton effect (at long wavelength) and a second negative one (at short wavelength) whereas addition of 1% of **3** induces the first negative and second positive Cotton effects, nearly symmetrically to the Cotton effect upon the addition of **2**. The 99:1 complexes show complementary Cotton effects at the same wavelength, and the opposite sign for each enantiomer, clearly indicating that predetermination of the helicity by a chiral trigger was successful. The CD spectra of 99:1 complexes and pure chiral gelators show Cotton effects and absorption maxima at different wavelengths, which clearly show that the Cotton effect of 99:1 complex is caused by induced helicity of an achiral gelator. The Cotton effects were shifted in the composite compared with the pure chiral compounds. This indicates that the packing mode is probably different in the composite and chiral gelators. There is a remarkable correspondence between the CD experiments and SEM observations. Microscopic insights from the CD experiments reveal that the chiral property of **2** and **3** can be reflected within the aggregates of achiral **1** without changing the helical structure derived from the aggregates of **1**. Macroscopic SEM observations also proclaim that the chiral property of the microscopic structure is preserved within the macroscopic structures without changing the original helical structure derived from **1**. This work reveals that a composition of only 1% of a chiral trigger can induce completely the helicity not only from the microscopic viewpoint, but also from the macroscopic structural viewpoint, in the gelation process.

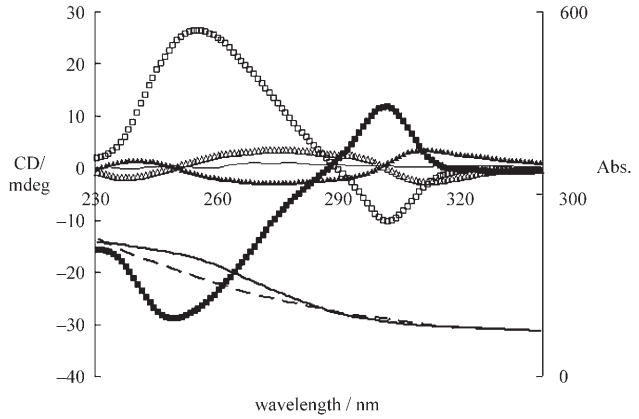

Figure 5. CD spectra of **1** (——), **2** (▲), **3** (△), **1/2** 99:1 (■) and **1/3** 99:1 (□). UV spectra of **1/2** 99:1 (-----) and **2** (——) in xerogel phase.

In conclusion, we have demonstrated the creation of well-defined homochiral helical ribbon structures in the gel phase. This is the first example of direct and complete control of microscopic and macroscopic helicity in gel phase, by the application of the sergeants-and-soldiers principle by using achiral gelator **1** and chiral gelators **2** and **3**. It is a unique system in that most of the sergeants-and-soldiers systems consisted of almost the same structure of chiral and achiral units, but we exploited chiral and achiral units with different structures. We expect that our results can be applied to the preparation of various types of homochiral nano- and microstructures by using different units of sergeants-and-soldiers in the gelation process.

Experimental Section

General method for the preparation of gels: Gelation tests were performed by solubilization of a weighed amount of gelator mixtures in a measured volume of selected organic solvent. The mixtures were heated until clear and cooled to room temperature. All the sample images were monitored using 10 mg gelator per 1 mL toluene (1.14% w/w). Samples for the xerogel images were dried in the air before examining SEM images. Organogels in the vial were carefully picked up and applied to the polymer or stainless steel stubs by a carbon tape.

Circular dichroism spectra techniques: Gel samples were sandwiched by two quartz plates and dried in the air for removal of toluene, because toluene is the UV-active solvent. Only xerogel phase CD experiments were performed. In order to rule out the possibility of the birefringency phenomena and intensity difference influenced by the sample thickness and measurement direction, the thickness of the samples were kept approximately the same and CD measurements were done several times in different directions by turning the sample.

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Keywords: gels · helical structures · nanostructures · self-assembly · sergeants-and-soldiers principle

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