

# Self-assembly of tris(phenylisoxazolyl)benzene and its asymmetric induction of supramolecular chirality†

Takeharu Haino,\* Masahiro Tanaka and Yoshimasa Fukazawa

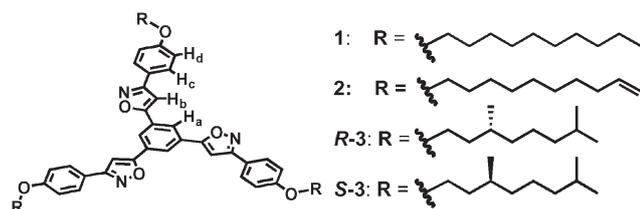
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Tris(phenylisoxazolyl)benzene stacks in a columnar fashion to form helical fibers that act as an organogelator, and the supramolecular chirality is asymmetrically induced in the presence of a tiny amount of a chiral source in solution.

Low-molecular-mass organic gelators with  $\pi$ -conjugated molecular structures represent remarkable examples of stacked molecular self-assemblies, which create one-dimensional nanostructured fibers.<sup>1</sup> The network coming from the one-dimensional nanostructured fibers can immobilize solvent molecules to increase the viscosity of organic media, and then an organogel forms. Such nanostructured morphology has attracted increasing interest, particularly for applications in nanomaterials and nanodevices.<sup>2</sup> The aggregation of the gelator molecules into a fibrous network is driven by multiple non-covalent interactions: coulombic, dipole-dipole, van der Waals, hydrogen bonding, and  $\pi$ - $\pi$  stacking. Mostly, a hydrogen bonding function and/or huge planar molecular surfaces need to be incorporated into a gelator molecule to produce fibrous gels.<sup>3,4</sup> There is a limited number of low-molecular-mass organic gelators that can assemble to form fibrous gels *via* weak intermolecular interactions:  $\pi$ - $\pi$  stacking, dipole-dipole, and van der Waals.<sup>5-7</sup> In this communication, we report a new class of low-molecular-mass organic gelators, tris(isoxazolyl)-benzene derivatives **1** and **2**, capable of self-assembling in a helical fashion, and asymmetric induction in the assembled state in solution. The molecules have three isoxazole rings, creating the directional arrangement of their local dipoles. Their one-directional circular arrangement facilitates  $\pi$ - $\pi$  stacking interaction along the  $C_3$  axis to form nanostructured fibers, which act as an organogelator.



The gelation ability of **1** was assessed in a variety of solvents. A suspension of **1** in acetone was heated to give a clear solution,

Department of Chemistry, Faculty of Science, Hiroshima University, 1-3-1, Kagamiyama, Higashi-Hiroshima, Japan.

E-mail: haino@sci.hiroshima-u.ac.jp; Fax: +81-82-424-0724;

Tel: +81-82-424-7427

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which was slowly cooled to room temperature. After leaving it for 1 h, a white gel formed and exhibited no gravitational flow, as it could be safely turned upside down. The gelation was entirely thermoreversible. Both **1** and **2** showed a high gelation performance in a variety of organic solvents: methylcyclohexane, ether, acetone, ethyl acetate, dimethyl sulfoxide and dimethylformamide, whereas 1,3,5-tris(4-decyloxyphenylethynyl)benzene **4**, possessing triple bonds instead of the isoxazole rings, did not form gels in those solvents. The critical gelation concentration varied in the range 0.8–3.5% wt/vol, depending on the solvents.

To gain an insight into the aggregation morphology of **1** and **2**, their xerogels were prepared on glass plates, and studied by field emission scanning electron microscopy (FESEM). The FESEM images in Fig. 1(a) and (b) show the three-dimensional networks responsible for the gelation. The aggregation of **1** formed well-developed cylindrical fibers with a diameter of about 200 nm.

A significant change in the morphology of the assembly was observed when the saturated alkyl ends of **1** were replaced by double bonds in **2** (Fig. 1(c) and (d)). The aggregation of **2** generated both right- and left-handed superhelical fibers with a diameter of about 3  $\mu\text{m}$ . The size of the superhelical fiber is 15 times as thick as that of **1**, suggesting that the terminal double bonds enhanced the further growth of the initial cylindrical assemblies *via* entwinement of the side chains. The superhelical fiber structure might suggest that the initial cylindrical assemblies of **1** and **2** should adopt a helical conformation.

Self-association of **1** was studied by  $^1\text{H}$  NMR and absorption spectroscopies. The  $^1\text{H}$  NMR signals of **1** are concentration-dependent in chloroform- $d_1$  (Fig. 2). Most of the signals shifted upfield upon increasing the concentration in a range of 0.163–200 mmol  $\text{L}^{-1}$ , whereas the proton signals of **4** showed no

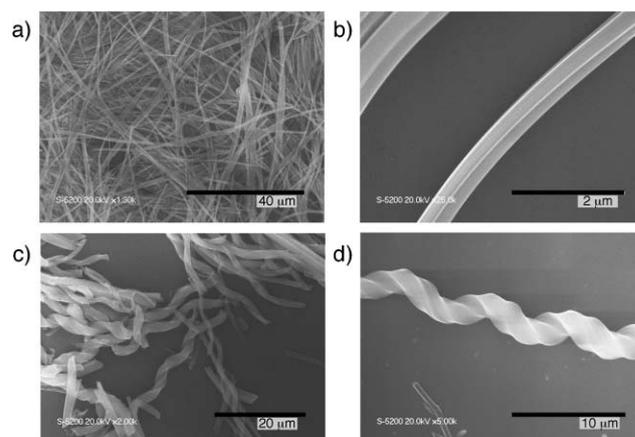
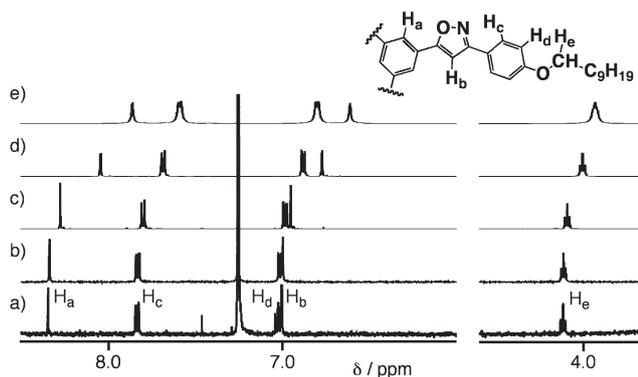


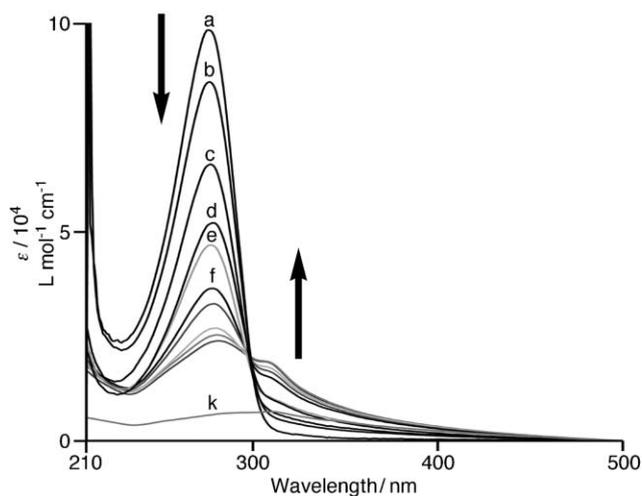
Fig. 1 FESEM images of xerogels of **1** (a and b) and **2** (c and d).



**Fig. 2**  $^1\text{H}$  NMR spectra of **1** at concentrations of (a) 0.163, (b) 1.98, (c) 16.8, (d) 100 and (e) 200  $\text{mmol L}^{-1}$  at 297 K in chloroform- $d_1$ .

concentration dependence. Obviously, the isoxazolyl group is a crucial incorporation for the self-assembly. Plotting the chemical shift changes of the protons vs. the concentrations of **1** produced hyperbolic curves. Non-linear curve-fitting analysis of the curves by applying the isodesmic model<sup>8</sup> produced the estimated complexation-induced shifts ( $H_a$ :  $-1.34$ ;  $H_b$ :  $-1.10$ ;  $H_c$ :  $-0.80$ ;  $H_d$ :  $-0.59$  ppm) and the association constant ( $K_a = 3.7 \pm 0.3 \text{ L mol}^{-1}$ ). The complexation-induced shifts decreased with increasing distance of the protons from the  $C_3$  axis of **1**, indicating that flat aromatic compound **1** stacks in a columnar fashion along the  $C_3$  axis.<sup>9</sup>

Absorption spectra of **1** provide supporting evidence for the formation of columnar aggregates. A diluted solution ( $0.001 \text{ mmol L}^{-1}$ ) of **1** displayed a sharp absorption band at 278 nm in methylcyclohexane (Fig. 3). The maximum peak in the absorption spectra clearly showed a red shift on increasing the concentration of the solution of **1**, and a new broad band gradually appeared around 310 nm. When the concentration of **1** reached  $1 \text{ mmol L}^{-1}$ , fibers formed, and the solution turned to a white suspension whose absorption spectrum showed a peak at 310 nm. Temperature-dependent absorption spectra show similar spectral features to those observed in the concentration-dependent measurements. Fluorescence spectra of **1** showed similar trends to



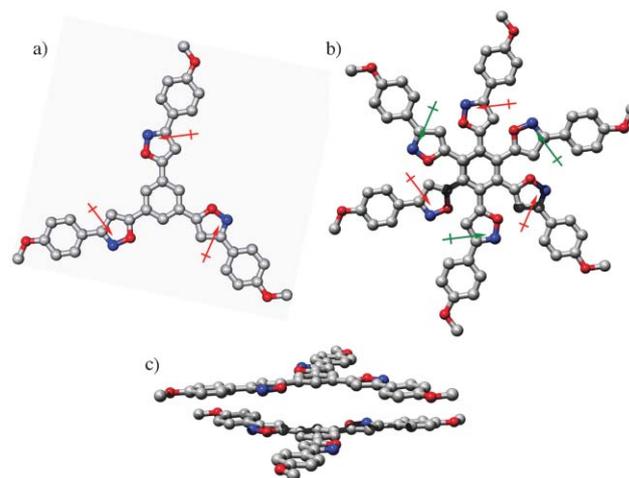
**Fig. 3** Electronic absorption spectra of **1** at concentrations of (a) 1.0, (b) 2.5, (c) 5.0, (d) 7.5, (e) 10.0, (f) 15.0, (g) 20.0, (h) 30.0, (i) 40.0, (j) 50.0 and (k)  $1000.0 \mu\text{mol L}^{-1}$  at 293 K in methylcyclohexane.

the absorption spectra, the value of the red shift being about 10 nm on increasing the concentration from  $0.001$  to  $1 \text{ mmol L}^{-1}$ . This suggests that the spectral changes originate from self-assembly of **1** into larger aggregates composed of  $\pi$ - $\pi$  stacked species. These observations were also matched by quantitative evaluation of the association constant achieved by fitting the data from the UV/Vis dilution studies to the isodesmic model<sup>8</sup> by non-linear least-squares regression analysis. The association constant was obtained for **1** ( $K_a = 180\,000 \pm 30\,000 \text{ L mol}^{-1}$ ). The value is very large compared with that in chloroform. It is apparent that solvophobic effects as well as stacking and dipole-dipole interactions play key roles in the formation of the larger aggregates.<sup>10</sup>

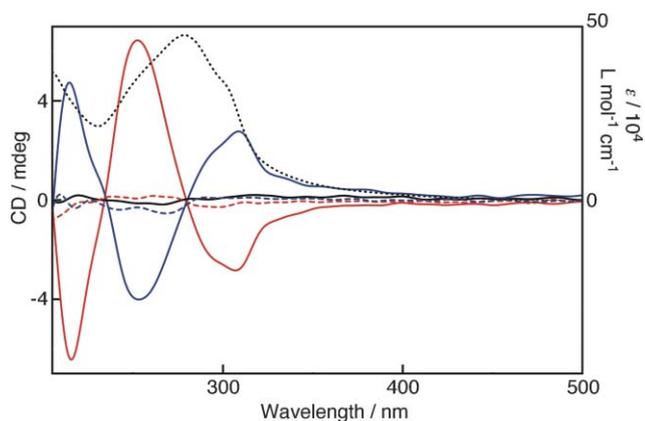
Molecular modeling of **1**, **1** and its partial structure, 3-(4-methoxyphenyl)-5-phenylisoxazole **5** by MO calculations using the DFT method (B3LYP/6-31G\*)<sup>11</sup> was carried out. Compound **5** has a fairly large dipole moment ( $\mu = 1.70 \text{ D}$ ), directed to the nitrogen atom along the  $\text{N}=\text{C}$  bond. The three isoxazole rings of **1** accept the circular array due to the local dipole interactions<sup>12</sup> (Fig. 4(a)); in fact, flipping one of the isoxazole rings to the opposite direction increased the total energy of **1** ( $\Delta E = 1.00 \text{ kcal mol}^{-1}$ ). The intramolecular circular array of the three dipole moments of course regulates the intermolecular arrangement of its self-assembled aggregate; the DFT calculation of **1** gave rise to the  $S_6$  symmetric structure (Fig. 4(b) and (c)), in which the six local dipoles of the isoxazole rings adopt a circular array, and **1** preferentially stacks in a columnar fashion due to rotational displacement of a neighboring molecule.

Supramolecular ordering of **1** can form helical columnar assemblies due to the intra- and intermolecular local dipole-dipole interactions. In the absence of a chiral source in **1**, the helical assemblies that are formed have both possible helical conformations ( $P$  and  $M$ ), having equal intermolecular interaction energies; thus, helical assemblies should exist as racemic mixtures. However, by means of the presence of a chiral source, the chemical equilibrium between  $P$  and  $M$  conformations can be biased on the higher supramolecular level of organization.<sup>13,14</sup>

Induced chirality of the supramolecular assembly of **1** was studied by circular dichroism (CD) spectroscopy in the presence



**Fig. 4** Calculated structures of **1** and stacked dimer **1**:**1**: (a) **1**, (b, c) top and side views of **1**:**1**. The arrows denote the local dipole moment of each isoxazole ring.



**Fig. 5** Circular dichroism spectra of **1** (solid black line,  $c = 0.1 \text{ mmol L}^{-1}$ ), **R-3** (dashed red line,  $c = 0.1 \text{ mmol L}^{-1}$ ), **S-3** (dashed blue line,  $c = 0.1 \text{ mmol L}^{-1}$ ), **1** ( $c = 0.1 \text{ mmol L}^{-1}$ ) with 0.01 mol% **R-3** (solid red line), **1** ( $c = 0.1 \text{ mmol L}^{-1}$ ) with 0.01 mol% **S-3** (solid blue line), and absorption spectrum of **1** (dashed black line) at 293 K in cyclohexane. All CD spectra were recorded in a  $1 \times 10 \times 45\text{-mm}^3$  quartz cell.

and absence of **3**. At a concentration of  $0.1 \text{ mmol L}^{-1}$ , the degree of polymerization can be estimated to be about 13–15-mers based on the association constant. CD spectra of achiral **1** with 0.01 mol% **R-3** and **S-3** were recorded at this concentration. Mirroring strong Cotton effects were observed upon the self-assembly of **1** whereas **3** gave rise to very weak Cotton effects at the same concentration as **1** due to its weak binding ability (Fig. 5). Remarkably, the supramolecular assembly displays optical activity in the CD spectrum despite only 0.01 mol% of chiral source **3** being present in solution. It is worth noting that the chiral information of a tiny proportion of the chiral source is transferred into the self-assembled columnar assemblies.

In summary, we have demonstrated that organogelators based on tris(isoxazoly)benzene assemble through only weak dipole-dipole and  $\pi$ - $\pi$  stacking interactions to create helical structures both in the gel and in solution, and the helical structures are influenced by an extremely tiny proportion of the chiral monomer on the overall helical conformation.

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