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Complementary hydrogen-bonding between thymidine-based low molecular-weight gelator and polynucleotide in organic media†

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We have found that aggregation mode and gelation property of thymidine-based organogelator 1 are affected by the addition of its complementary polynucleotide in organic media.

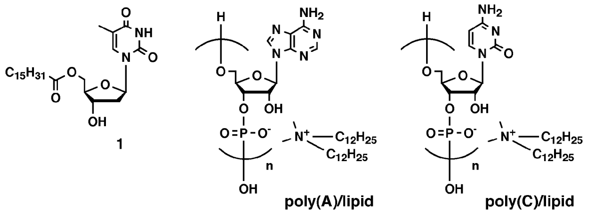
Motivated by many potential applications of gels based on supramolecular chemistry, development of new low molecular-weight gelators for organic solvents and investigation of their attractive self-assembling properties have recently received much attention.[1] Prebiotic molecules such as amino acid derivatives,[2] carbohydrates,[3] lipids[4] and steroids[5] are known to be useful as the scaffolds to design low molecular-weight gelators because they are applicable to cosmetics, foods, medicines, sensors and so forth with biodegradable and biocompatible properties.[6]

Despite the recent achievements elucidating the molecular prerequisites for gelation ability using prebiotic molecules,[3,7] the control of these aggregation structures and properties is still a challenging goal. So far, however, only a few attempts have been made to achieve this purpose by the combination of low molecular-weight gelators with a function related to molecular recognition.[8] Without doubt, the most attractive molecular recognition event in biomolecules is that observed for nucleobases. Herein we report on a drastic change in aggregation morphology and gelation properties of nucleoside-based gelator,[9–11] induced by the complementary hydrogen-bonding with RNA.

Kim *et al.* have already reported a family of thymidine-based organogelators and found that some of them show good gelation abilities toward nonpolar solvents.[10] For example, 5′-esterificated thymidine derivative (**1**) aggregates through the hydrogen bonding interaction, van der Waals interaction and π–π stacking, and forms organogels with benzene, toluene, CCl_4, tetrahydronaphthalene (THN), hexane and cyclohexane. We first tried to add complementary polymer [in this case: poly(A)] into **1** gel phase, however, it was virtually insoluble in such nonpolar solvents. To dissolve poly(A) into organic media, we prepared poly(A)/lipid by an ion-pair exchange with a cationic surfactant: didodecyldimethylammonium bromide (DDAB).[12] Poly(C)/lipid was prepared as a non-complementary polynucleotide.

Interestingly, when an equal amount of poly(A)/lipid was dispersed within **1**/benzene gel and the mixture was heated to obtain the sol phase, the opaque gel of **1** was turned into the transparent gel by cooling (Fig. 2a). In contrast, the original opaque gel was obtained from **1** with poly(C)/lipid. It is possible that macroscopic aggregation structure is changed by the addition of poly(A)/lipid forming the complementary hydrogen-bonding.

The hydrogen-bonding interaction is one of the major driving forces for gelation of **1**. We thus measured ATR-FTIR spectra to confirm the change in hydrogen-bonding mode by the addition of polynucleotide (Fig. 1). A characteristic peak of **1** gel at 3431 cm^{-1}, which is attributed to hydrogen bonding 3′-OH,[10] disappeared by the addition of poly(A)/lipid. The contribution of A–T base pairing can be easily discussed by the C=O stretching band appearing around 1650–1700 cm^{-1}. Poly(A)/lipid did not show such a peak around this wavenumber region. In **1** gel, a strong peak at 1659 cm^{-1} was decreased whereas that at 1694 cm^{-1} was increased by adding poly(A)/lipid, indicating that non-complementary T–T



Scheme 1 Structures of thymidine-based organogelators (**1**), its complementary polymer: poly(A)/lipid and non-complementary poly(C)/lipid.

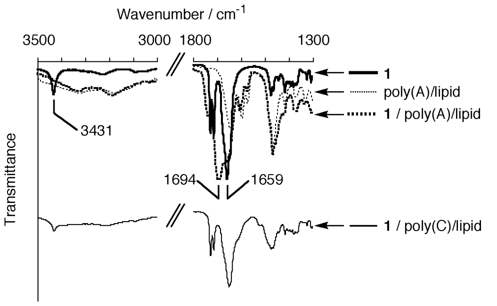


Fig. 1 ATR-FTIR spectra of dried samples obtained from **1** gel (bold line), **1** with poly(A)/lipid gel (bold dotted line), poly/(A)lipid (dotted line) and **1** with poly(C)/lipid gel (thin line). Poly(A)/lipid and poly(C)/lipid were added 1.0 equivalent with respect to **1** (nucleobase unit): [A or C]/[T] = 1.0.

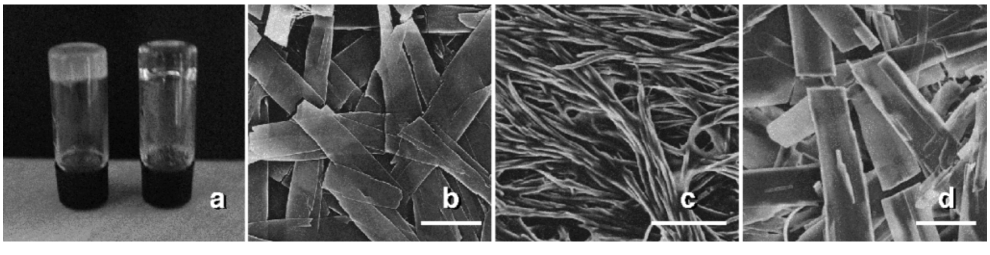


Fig. 2 (a) Photograph of **1** gel (left) and **1** with poly(A)/lipid gel (right); SEM images of (b) **1** gel, (c) **1** with poly(A)/lipid gel and (d) **1** with poly(C)/lipid gel, prepared from benzene, bar length = 5 μm, [A or C]/[T] = 1.0.

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† Electronic supplementary information (ESI) available: IR spectral changes in **1** gel induced by poly(A)/lipid addition; TEM images of **1** gel and **1** with poly(A)/lipid (1.0 eq.) gel, and SEM image of **1** with poly(A)/lipid gel (0.5 eq.). See http://www.rsc.org/suppdata/cc/b4/b407756n/

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hydrogen-bonding pairs or 3′-OH–T hydrogen-bonding are reassembled to complementary A–T hydrogen-bonding pairs.[13] On the other hand, IR spectrum of **1** with poly(C)/lipid gel was much the same as that of **1** gel, indicating that poly(C)/lipid does not interact with **1**. Since the IR spectral change by the addition of poly(A)/lipid was saturated at around 1.0 equivalent, the stoichiometry between A and T should be 1.0 as in the case of Watson–Crick base pairing (ESI: Fig. S1).†

To examine the aggregation structure of **1** in the gel phase, we took electron micrograph (SEM and TEM) images. In **1**/benzene gel, the plate-like crystalline structure was observed as already reported for related thymidine-based organogelators (Fig. 2b).[10] As expected from foregoing gel turbidity and IR spectral similarity, the plate-like structure was also observed for poly(C)/lipid gel (Fig. 2d).[14] Interestingly, this plate-like structure was torn into shreds by the addition of poly(A)/lipid and the 3-D entangled fiber structure was observed (Fig. 2c). The morphological changes of **1** gel were also saturated at around 1.0 equivalent of poly(A)/lipid (Fig. S2).

The crystallinity of the aggregate in the gel phase is an important point affecting the bulk gelation property. One can notice from the SEM image of **1** with poly(A)/lipid gel that the surface is rough and the fiber structure entangled windingly; that is, crystallinity is low. We also confirmed that X-ray diffraction (XRD) peak intensities of **1** gel are decreased by adding poly(A)/lipid (Fig. 3). This result indicates that poly(A)/lipid prevents the bilayer assembly structure of **1** (inset figure in Fig. 3) from growing up to multi-layers.

To evaluate the bulk gelation property, we measured the gel-to-sol phase transition temperature (T_{gel}, [**1**] = 2.0 wt/vol%, [A or C]/[T] = 1.0, benzene). The vial containing the gel was immersed inversely in a thermo-controlled oil bath, and the temperature was increased in the rate of 1 °C min^{-1}. When the gel collapsed, we defined the temperature as T_{gel}. **1** gel and **1** with poly(C)/lipid gel were heavily turbid and gradually spilled the solvent out between 40 to 70 °C. These phenomena are often seen for the crystalline gel. In contrast, **1** with poly(A)/lipid gel was beautifully transparent and a sharp gel-to-sol phase transition temperature appeared at 60 °C. This result indicates that bulk property and stability of the present gel system are controlled by the complementary hydrogen-bonding. In fact, we noticed that **1** gel is stabilized against mechanical shaking by the addition of poly(A)/lipid.

In conclusion, we have demonstrated that a thymidine-based organogelator (**1**) interacts with complementary poly(A)/lipid in the gel phase and the drastic changes in aggregation morphology and gelation properties are induced. Although only a few attempts to combine nucleobase-appended gelators with its complementary DNA or RNA have been reported,[15] these systems were limited to aqueous media because of the solubility problem in DNA and RNA. In this report, we found that poly(A)/lipid acts as a modifier for gelation properties in organic media where the hydrogen-bonding interaction can exert the very strong attractive force. We believe that the present organogel system should be more general to combine low molecular-weight gelators with polymeric compounds utilizing a concept of molecular recognition.

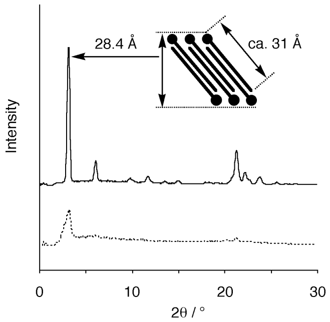

Fig. 3 X-ray powder diffraction diagrams of **1** gel (solid line) and **1** with poly(A)/lipid gel (dotted line): [**1**] = 2.0 wt/vol%, [A]/[T] = 1.0. Inset figure shows a possible molecular arrangement of **1**.

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[14] We observed only small amount of entangled fiber structure in **1** with poly(C)/lipid gel, however, almost all of the sample were plate-like structure as shown in Fig. 2d.

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