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Synthesis of organogelling, fluoride ion-responsive, cholesteryl-based benzoxazole containing intra- and intermolecular hydrogen-bonding sites

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ABSTRACT

A cholesteryl-based 2-(2′-hydroxyphenyl)benzoxazole (HPB) derivative **3** linked with an amide bond was prepared through an efficient synthetic pathway. The HPB, amide, and cholesteryl groups play important roles in constructing the supramolecular gel structure. UV–vis and fluorescence spectroscopy also showed that HPB and amide groups, which provide intra- and intermolecular hydrogen bonding, respectively, also contribute the recognition of fluoride anions.

The self-assembly of functional small molecules into the supramolecular structure is an interesting approach to the development of new nano-scale materials.[1] Recently, low molecular weight gels organized in nano-architectures through specific noncovalent interactions, such as hydrogen bonds, π–π interactions, and van der Waals forces have attracted considerable attention as an elegant class of self-assembled materials.[2] In particular, organogelators have attracted significant interest for their potential applications including sol-to-gel transcription,[3] switching properties,[4] organic light emitting diodes,[5] transistors,[6] and light harvesting materials.[7]

Interestingly, organogels based on low molecular weight compounds with the receptor moiety or photo-functional groups have been the target of increasing attention because of the wide range of potential field-responsive applications, such as light-responsive properties,[8] complexation,[9] and sensing.[10] Regarding the sensing properties, photo-responsive organogels are subjected to change in their suprastructure and fluorescence in response to external physical and chemical stimuli.[11]

As a type of intriguing building block, urea and amide groups are used widely as elements for fluorescent receptors as well as for the supramolecular architecture based on intermolecular hydrogen bonding.[12] Similar to urea and amide groups in the gelling system, HPB exhibits exciting anion-responsive properties and provides intra- and intermolecular hydrogen bonding sites for supramolecular structuring.[13] However, recent reports on the organogelling systems containing HPB are rare. HPB molecule generally exists as an enol tautomer with a short-wavelength emission. Once irradiated, the HPB molecule transforms into a keto tautomer with a long-wavelength emission via an excited state intramolecular proton transfer (ESIPT) process (see Scheme S1 in the Supplementary data).[14] Intramolecular hydrogen bonding in HPB and intermolecular hydrogen bonding in the amide group can be altered by the presence of fluoride anions regardless of its monomeric or polymeric form, which showed a visually noticeable color change.

In this study, organogelators **3** containing a cholesteryl group with a fluorophore (HPB) linked with an amide group was designed and synthesized, as illustrated in Scheme 1. The synthetic strategy stems from the fact that a cholesteryl-based amide with a strong intermolecular hydrogen bond and van der Waals forces may provide powerful driving forces to form an organogel.[14d] Moreover, the introduction of an HPB unit into such a system can help to facilitate intermolecular forces via π–π interactions. Such interactions might induce the self-assembled gelation leading to a supramolecular architecture.

The details of the synthesis of compound **3** are described in the Supplementary data. Organogelator **3** was synthesized using a simple and easy method. Compound **3** can form a gel only in a mixture of cyclohexanone and cyclohexane or cyclohexane and *p*-xylene. Solvent mixtures were employed as the gelation medium because no sole solvent was found to be efficient for gelation. A feature of compound **3** is the readily-induced gelation in solvent mixtures through a heating–cooling method, providing a new fluorescent supramolecular system (Fig. 1). The organogel of compound **3**

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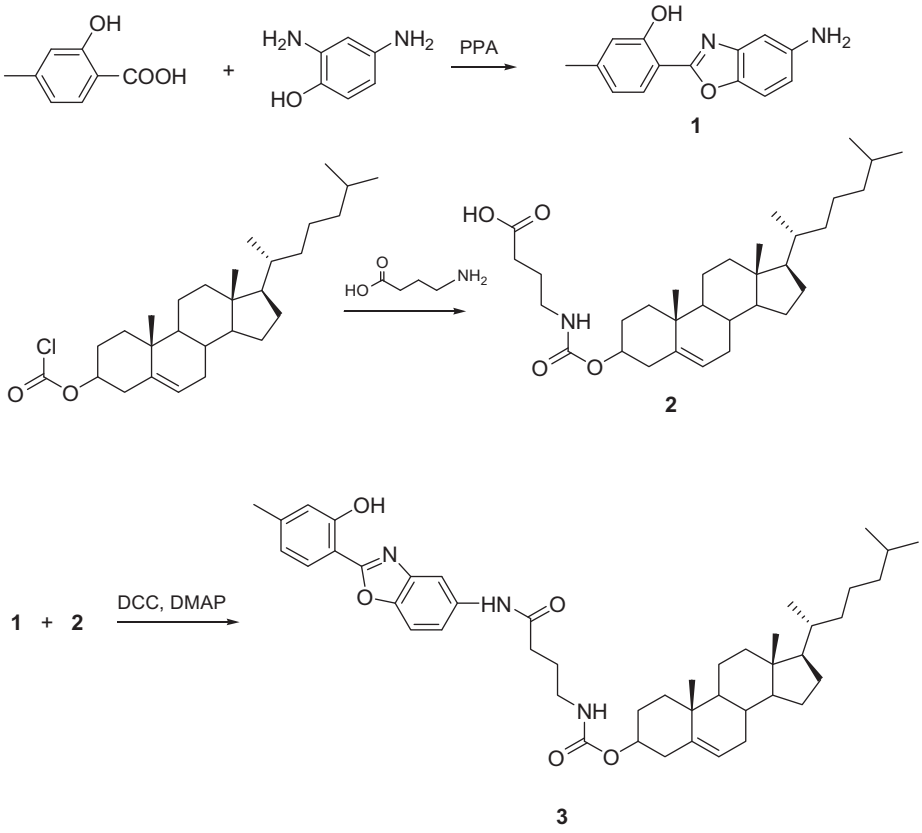

Scheme 1. Synthetic route of organogelator **3**.

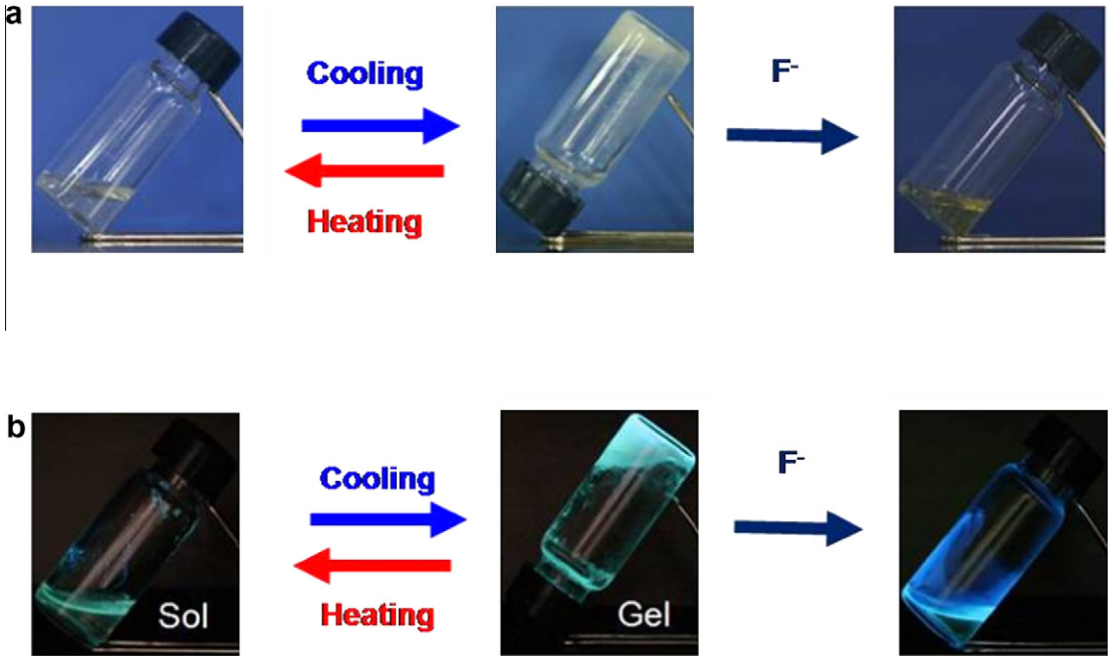

Figure 1. Photographs of the sol-to-gel process of compound **3** under (a) ambient light and (b) UV-irradiation and the effect of fluoride anion.

was stable for months and the sol-to-gel transitions were thermally reversible. The critical gelation concentration and gel-to-sol transition temperature of compound **3** in the cyclohexanone and cyclohexane mixture were 28 mg/mL and 53 °C, respectively.

The self-assembled gel structure of xerogel of compound **3** from the solvent mixtures was examined by field-emission scanning electron microscopy (FE-SEM). The FE-SEM images of the gel from cyclohexanone and cyclohexane (1:3, v/v) show that the gel had

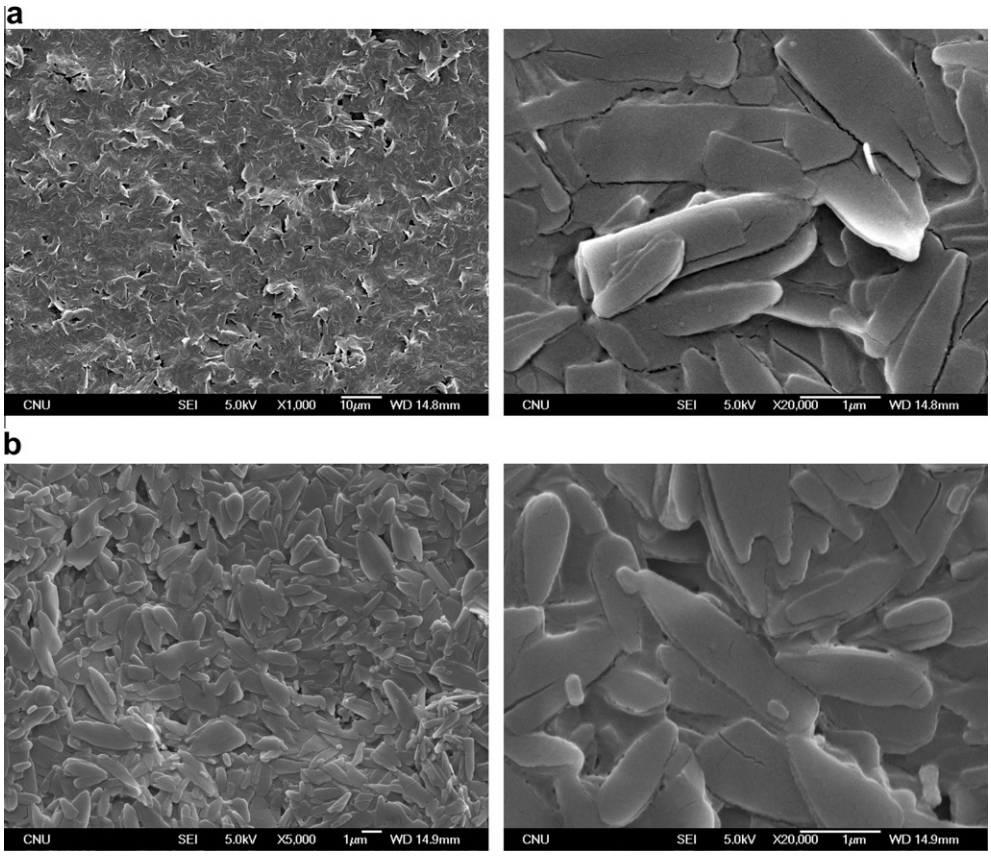

Figure 2. FE-SEM images of the xerogel of compound **3** from (a) cyclohexanone/cyclohexane (1:3, v/v) and (b) cyclohexanone/*p*-xylene (1:3, v/v).

leaf-like aggregation with a length and width of approximately 2 μm and 0.3–0.8 μm, respectively (Fig. 2a). The xerogel from the mixture of cyclohexanone and *p*-xylene (1:3, v/v) has a similar morphological structure and size to that from the mixture of cyclohexanone and cyclohexane (Fig. 2b). Hence, cooperative interactions between molecules, such as hydrogen bonding, van der Waals force, and π–π interactions facilitate the formation of the self-assembled gel architecture.

The UV–vis absorption and emission spectra of compound **3** in a dilute chloroform solution (1.0×10^{-5} M) were investigated (Fig. 3a). Compound **3** emits a bluish green fluorescence at the maximum wavelength of 484 nm resulting from the keto form via ESIPT under excitation of 330 nm in a chloroform solution. Along with the emission at 484 nm, short wavelength emission at 388 nm was also observed due to the enol tautomer of **3**. This means that the ESIPT can develop in a chloroform solution, whereas it is inefficient for gelation because of the excellent solubility.

The ESIPT process in compound **3** was examined by the concentration-dependent emission spectra in a mixture of cyclohexanone and cyclohexane (1:3, v/v) as shown in Figure 3b. As the concentration of compound **3** increased from the solution to gel state through an aggregated state, the long-wavelength emission at 491 nm was intensified due to the facilitated ESIPT process in the solid state. Compared to the emission spectra in chloroform shown in Figure 3a (keto form dominant), the enol tautomer is dominant in the dilute solution (cyclohexanone and cyclohexane) with a concentration of 0.01 wt %, presumably due to the effect of the solvent polarity.[14c,15] Based on this, free rotation between the benzoxazole and phenol group is possible resulting in dominant enol tautomer. However, the free rotation between the benzoxazole and phenol group was inhibited by the formation of a planar keto tautomer at a more concentrated condition, resulting in the spontaneous gelation through enhanced π–π intermolecular interactions (inset structures in Fig. 3b).

Based on the role of intramolecular hydrogen bonding in the ESIPT mechanism, compound **3** showed a spectroscopic response upon the addition of fluoride ions with compound **3** in the gel state. The addition of tetrabutylammonium fluoride resulted in a rapid transition from an opaque gel to a homogeneous solution with an altered fluorescence color (Fig. 1). The solution did not return to a stable gel. This means that some driving forces for gelation were affected by the presence of a proton-attracting fluoride anion. As already reported, the N–H bond in the amide group interacted with a fluoride ion via hydrogen bonding or was deprotonated by the presence of fluoride ions resulting in a disruption of the gel state.[16]

The interaction between compound **3** and fluoride anions in a DMF solution was examined by UV–vis and emission spectroscopy. As shown in Figure 4a, compound **3** has a high selectivity toward fluoride ions, as determined from the colorless to yellow color change that could be observed by the naked eye, exhibiting a red-shift in absorption from 332 to 410 nm. In contrast, the UV–vis spectra showed a negligible change after the addition of other anions, such as chloride, bromide, iodide, and acetate.

The emission spectra were obtained with the excitation of compound **3** at 333 nm. As shown in Figure 4b, the fluorescence spectra changed considerably upon exposure to fluoride ions. A unique emission band appeared at 450 nm with a shoulder at 418 nm, while other ions did not show any noticeable change in emission band except for acetate ions. It was assumed that the conjugation and electronic environment for intramolecular hydrogen bonding

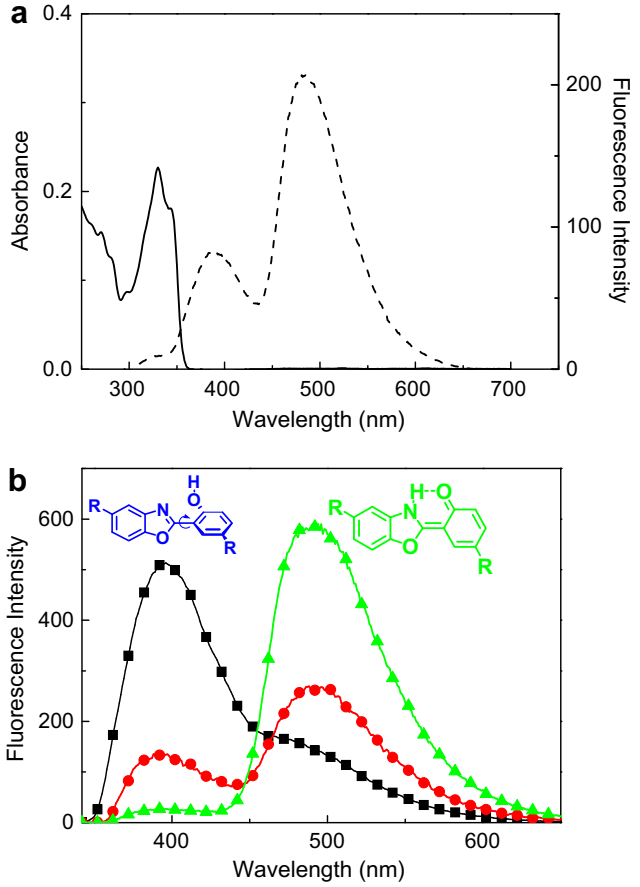

Figure 3. (a) Absorption (solid line) and emission spectra (dashed line) for compound **3** in chloroform (1.0×10^{-5} M, excitation wavelength at 330 nm); (b) emission spectra of compound **3** at different concentrations in cyclohexanone/cyclohexane (1:3, v/v) solution (λ_{ex} = 332 nm); concentration of **3** = 0.01 wt % (solution, ■), 0.1 wt % (aggregated state, ●), and 10 wt % (gel state, ▲).

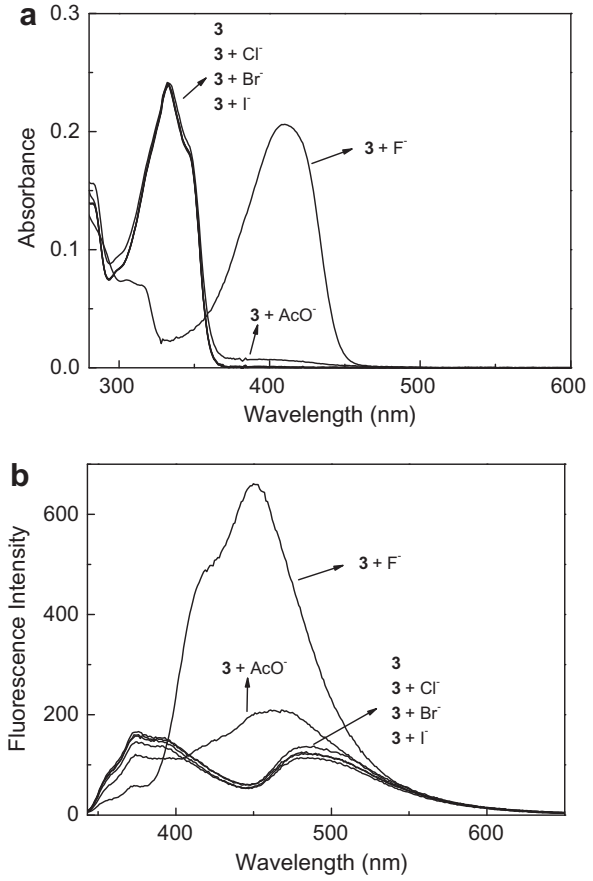

Figure 4. (a) Absorption and (b) emission spectra of compound **3** in a DMF solution upon the addition of variuos anions; [**3**] = 1.0×10^{-5} M and [anion] = 1.0×10^{-3} M; excitation wavelength 333 nm.

between N–H and O=C might be affected by fluoride anions, which is responsible for the shift in the two emission bands. This suggests that intramolecular hydrogen bonding-induced ESIPT is practically disabled due to the interruption of fluoride ions.

The fluoride ion-responsive property of compound **3** can be explained by the following: (i) a change in intermolecular hydrogen bonding between the amide bonds, which is an intriguing driving force for gelation, resulting in a gel-to-sol transition; and (ii) a change in intramolecular hydrogen bonding between N–H in bezoxazole ring and O=C in phenylene unit, which are important constituents for ESIPT, resulting in a disabled ESIPT-exhibiting superimposed emission.

In conclusion, organogelator **3** was synthesized using the core structure of a HPB ring linked with an amide bond and cholesteryl group at the end to provide a π–π interaction, intermolecular hydrogen bonding, and van der Waals force during gelation. Compound **3** exhibited fluorescence spectra suitable for the ESIPT mechanism upon a sol-to-gel transformation due to the dominant keto tautomer upon gelation. Upon exposure to fluoride anions, gelled compound **3** transformed into a transparent solution due to a disruption of the intermolecular forces.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.08.053.

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