

Versatile Supramolecular Organogel with Outstanding Stability toward Aqueous Interfaces

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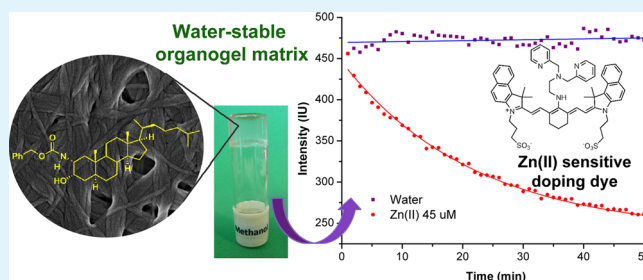
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S Supporting Information

ABSTRACT: In this communication, we report on a novel and versatile low-molecular-weight organogelator. The methanolic gel exhibits an exceptional water-enhanced stability as evidenced by a 30 °C increase in T_g with up to 10%v/v of water. This atypical property not observed with other solvents makes of this supramolecular gel a highly stable matrix compatible with aqueous interfaces. As a proof of principle we present the sensing performance of a symmetric tricyanocyanine fluorophore bearing a Zn(II)chelator unit. The system retained its remarkable physical integrity for a long period of time opening new possibilities for other organic–aqueous interface applications.

KEYWORDS: supramolecular, organogel, sensing, tricyanocyanine, aqueous interface



During recent years, the increasing research on materials science has shown the potentiality of functional gels for a wide variety of high-tech applications, from regenerative medicine to electronic devices and/or media for chemical reactions and sensing, etc.^{1,2} Gels are materials formed mostly by liquid, yet they rheologically behave like solids because of a three-dimensional network that entraps and immobilizes the fluid. In comparison to traditional polymeric gels, viscoelastic materials made of low-molecular-weight organic gelators (LMOGs) show the ultimate level of innovation in this area, by means of a better-defined mode of self-assembly than the former and the reversibility of their self-assembled fibrillar network (SAFIN). LMOG compounds self-organize through supramolecular, noncovalent interactions, to form gels in water (hydrogel), organic solvents (organogel) or ionic liquids (ionogel)³ that can be sensitive to a variety of physical (temperature, light, etc.) and/or chemical (pH, ions, etc.) stimuli.^{4,5} Modification and design of LMOGs are easier than those on polymers. In addition, drug-doped gels may be simply prepared by adding the drug (biologically active compound for drug delivery systems, fluorescent dyes for sensing systems, etc.) during the organogel preparation making it possible to have precise control of drug concentration. In the past decade the development of fluorescent gels has been an important field of research, according to their potential applications for the preparation of optoelectronic devices and sensors.⁶ Fluorescence emission as a tool to evidence the presence or absence of a particular analyte is one of the most widespread methods applied in different fields providing detection with unique sensitivity and selectivity.⁷ In fluorescent supramolecular gels,

the organic fluorophore molecule may be a gelator by itself,⁸ or entrapped between the fibrillar network of a known LMOG.^{9,10} Such systems have already been used as sensors for a variety of organic molecules,^{11–13} ions¹⁴ and gases.¹⁵ Nevertheless, those that have been reported as a suitable media for ion sensing in aqueous interface are mainly hydrogels.¹⁶ The use of organogels as sensors in aqueous media is limited because of the following factors: (a) impermeability of the organogel to water or (b) when permeable, the presence of water, or even alcohols, usually breaks the gel by disrupting the fibrillar network through hydrogen bond interactions leading to a gel–sol transition. We report on the synthesis and characterization of a new cholesterol-derived LMOG **1** (Figure 1) with a broad gelation scope ability and we demonstrate that the stability of the alcoholic organogel is enhanced by the presence of water. As a proof of principle for the use of these gels as outstanding stable matrix in aqueous interface, we present the performance of the organogel doped with the near-infrared fluorescent symmetric tricyanocyanine **2** for detection of micromolar levels of Zn(II) in aqueous interface.

In our search for new supramolecular organogelators, we have recently synthesized steroid **1** from cholesterol in a seven-step synthetic route (see the Supporting Information). This relatively simple molecule with a carbamate moiety turned out to be an excellent organogelator for a wide variety of solvents, being capable of gelling 20 out of 35 tested solvents. LMOG **1**,

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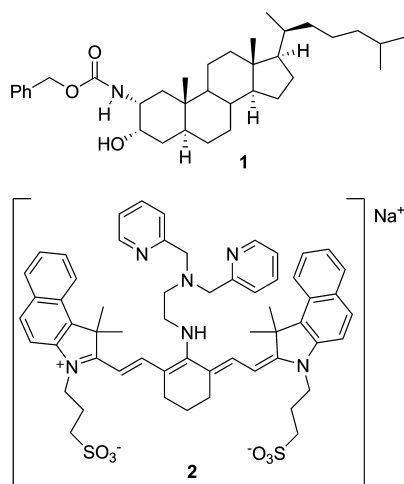


Figure 1. Structures of LMOG 1 and fluorescent sensor 2.

a superorganogelator for hydrocarbons with a critical concentration for gelation (CCG) of 0.06% w/v for *n*-decane and 0.2% w/v for cyclohexane, was also capable of forming stable gels in polar solvents such as ethyl acetate, acetonitrile, DMF, and even small alcohols (methanol, ethanol, and *n*-butanol), but it did not form hydrogels because of its low solubility in water. Detailed gelation behavior and CCG of the complete set of solvents is shown in Table S2 of the Supporting Information. The morphology of the xerogels from methanol, acetonitrile, and *n*-hexane were analyzed by SEM microscopy. The images showed a typical entangled fibrillar network with fibers with a minimum width of 40 nm and lengths up to several micrometers (for images see the Supporting Information). FT-IR spectroscopy of the gel and sol of **1** in xylene, which is inert to hydrogen bonding, provided evidence that the self-assembly mechanism involves the protons of the hydroxyl group and the carbamate moiety through hydrogen bond interactions. In a hot xylene solution, two single broad bands were observed at 3584 and 3449 cm^{-1} for the free O–H and N–H stretching; as the solution cooled down and the sample started to gel, the two bands appeared shifted to 3489 and 3344 cm^{-1} , typical of intermolecular hydrogen bond. When the sample reached room temperature, the original stretching bands of free O–H and N–H had completely disappeared. Usually, hydrogen-bond-directed self-assembled fibrillar networks break down in the presence of protic solvents as water or alcohols.¹⁷ The fact that LMOG **1** is also capable of gelling alcohols indicates that the intermolecular hydrogen bonding directing the self-assembly is strong enough to prevent gel to sol transition by solvation with the protic solvent. LMOG **1** can also selectively gelate the organic phase of a mixture of water and hydrocarbons (for example, *n*-hexane, and petrol, see the Supporting Information) with possible applications on containing oil spills.¹⁸ Methanol/water mixtures were also tested as gelation solvents and, unexpectedly, the gels obtained were more stable than those with pure methanol. To estimate the relationship between thermal stability, concentration of gelator and nature of the solvent we studied the variation of the gelation temperature (T_g) with the concentration of **1** in gels of ethyl acetate, acetonitrile, methanol, and methanol/water mixtures. Tube inversion experiments were performed to measure the T_g .¹⁹ In all cases, as the concentration of **1** was increased, T_g also increased. The methanol–water mixture showed an almost linear relationship between T_g and LMOG

concentration. An enhanced thermal stability of the gels was reflected in a 30 °C increase in T_g values from 56 °C in methanol to 86 °C for a 90:10 methanol:water mixture for a 1.6% w/v LMOG **1** (Figure 2). This stabilizing effect is also

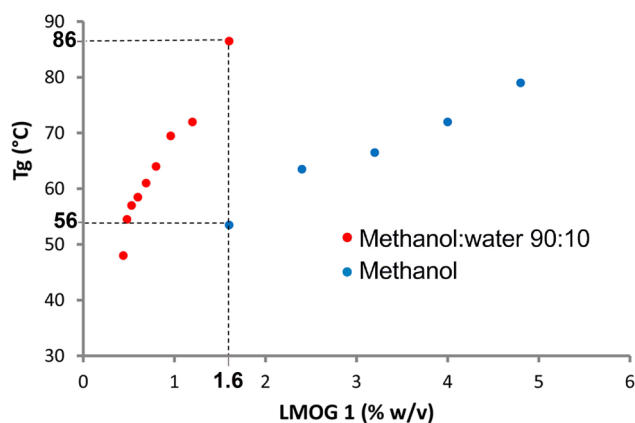


Figure 2. T_g vs LMOG concentration plots for methanol (blue) and methanol with 10% of water (red).

observed when water is added over a methanolic gel of **1** and diffuses into the gel. The CCG in the 90/10 methanol/water mixture decreased to 0.44%w/v, in agreement with a stronger fibrillar network in the presence of water.

Because gelator **1** is not soluble in water, the addition of a proportion of water to the gelled solvent would decrease the solubility, thus enhancing the strength of these gels. Nevertheless, this stabilizing effect is not general because addition of 10% of water to acetonitrile did not enhance the strength of the gel obtained (T_g 70 °C 1.2 wt % of **1**). The unusual methanol/water-stabilizing effect observed turns this gel into a highly stable matrix toward aqueous interfaces with many potential applications such as, for example, a support for sensing water-soluble analytes like ions or biomolecules in aqueous interfaces by means of an adequate sensitive fluorophore dopant. As a proof of principle, we studied the sensing performance of **2** (Figure 1), derived from a symmetric tricyanocyanine dye. The probe bears in its chemical structure a fragment of *N,N*-di(2-picolyl)ethylenediamine (DPEN) as the metal chelator unit for zinc ion. The sensitivity of the chelation and the selectivity for zinc among other metals was previously studied by our group, as well as the versatility of tricyanocyanine parent structure to obtain a wide variety of NIR-probes.²⁰ The sensor **2** is completely soluble in methanol and water. This is a very important property when it comes to the incorporation of the dye in the organogel because it ensures a homogeneous dispersion of the fluorophore before gelation precluding any possibility of precipitation after contact with the aqueous interface. T_g values of the dye-doped gel showed no variation with regard to the nondoped gel indicating that fluorophore **2** is not located in the fibrils but solubilized between the cavities of the fibrillar network. Regarding its optical characteristics, the tricyanocyanine has a sufficient fluorescence quantum yield to allow doping with low levels of concentration within the gel. Moreover, as it was observed with other fluorophores⁸ the emission intensity is enhanced within the gel matrix in comparison with the intensity at the same concentration in solution (see page S16 in the Supporting Information). The chances of dye aggregation within the gel matrix with consequent dye self-quenching are significantly reduced in the

working conditions ($2.8 \mu\text{M}$). Another important aspect is that this sensor is a near-infrared fluorophore, a high-rated property to achieve deep penetration in the sample and to reduce to almost minimal levels the emission produced by autofluorescence of some relevant targets like biomolecules. The fluorophore **2** has also a large Stokes shift ($>100 \text{ nm}$) a very interesting and desirable property for fluorescent probes to minimize interference of excitation light or autoabsorption phenomena. The effect of adding zinc ion to a solution of **2** in water is a decrease of the emission intensity at 785 nm and a 20 nm bathochromic shift of the maximum.²⁰ The transparency of the methanolic gel allowed us to perform the fluorescence measurements using the right angle technique. Within the 1.5% organogel, sensor **2** shows an emission maximum at 782 nm , which undergoes a decrease in the intensity over time when it is in contact with an aqueous interface containing a range from 5 nM to $45 \mu\text{M}$ in Zn(II) . Each condition was monitored for at least 50 min acquiring an emission spectrum every minute. A blank control was carried out in the same condition with an aqueous interface lacking of zinc ion (Figure 3). The highest

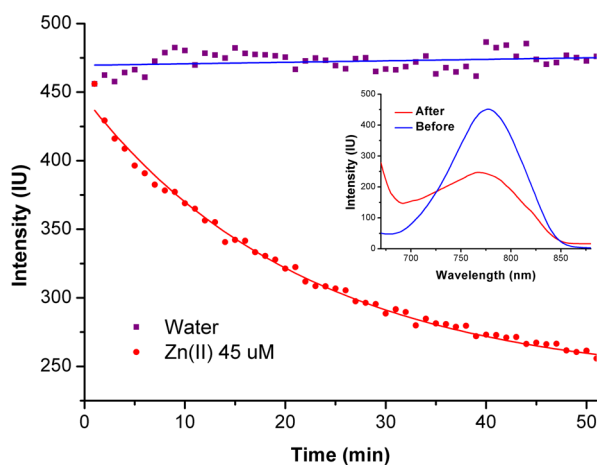


Figure 3. Comparison of the corrected fluorescence emission of the cyanine ($2.8 \mu\text{M}$, $\lambda_{\text{ex}} 650 \text{ nm}$) in the organogel from methanol (1.5% w/v) along 50 min after the addition of $50 \mu\text{L}$ of water (blue) and $50 \mu\text{L}$ of the $45 \mu\text{M}$ Zn(II) aqueous solution (red). Inset: Fluorescence spectra of the cyanine ($2.8 \mu\text{M}$, $\lambda_{\text{ex}} 650 \text{ nm}$) in the organogel from methanol (1.5% w/v) before (blue) and 50 min after the addition of $50 \mu\text{L}$ of the $45 \mu\text{M}$ Zn(II) aqueous solution (red).

quenching efficiency was 35% at a zinc ion concentration of $45 \mu\text{M}$. In order to compute a dissociation constant (K_{D}) for the sensor/zinc binding within the gel, the percentage of quenching at 782 nm at 45 min after exposure to the aqueous interface was plotted against zinc ion concentration (Figure 4) and fitted with a single exponential curve. The computed K_{D} value is $25.4 \mu\text{M}$, as expected, higher than that of the same DPEN- Zn(II) pair in solution (300 nM),²⁰ probably because of the influence of the diffusional factor which is not negligible within the gel. However, we consider this preliminary computed value a very interesting result because of the dynamic range of detection that could be considered when using the gel as a sensor device. Moreover, the outstanding stability of the macroscopic structure of the organogel in an intimate contact with the aqueous interface for a long period of time (50 min) stimulates the potentiality of this organogel as a medium for organic–aqueous interface applications.

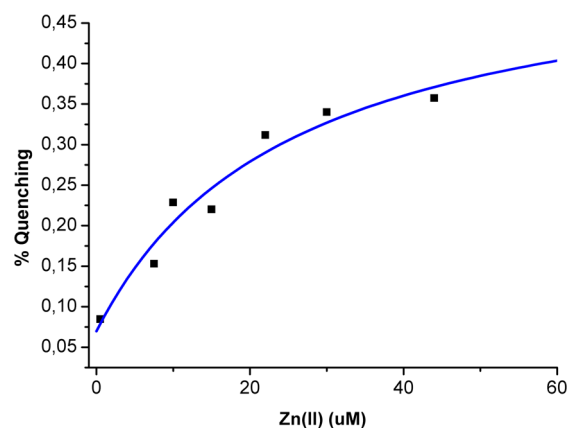


Figure 4. Fluorescence quenching percentage versus concentration. The binding constant in the organogel was calculated by fitting the exponential curve.

In summary, we report on the synthesis and characterization of a new cholesterol-derived low molecular weight gelator capable of gelling a wide variety of solvents with a remarkable water stabilizing effect. The FT-IR analysis of the gelling process revealed that two hydrogen bond interactions are involved in the supramolecular self-assembly. The organogels are ultrastable in contact with an aqueous interface and, in the case of methanolic gels, the diffusion of water into the self-assembled fibrillar network enhances the stability by increasing the T_{g} and decreasing the CCG. This result prompted us to investigate the use of this gel as a matrix for ion sensing in aqueous interface using cyanine **2** as a selective sensor for Zn(II) . The system shows a dynamic range for sensing between 5 nM and $45 \mu\text{M}$ of the Zn(II) aqueous solutions with a dissociation constant of $25.4 \mu\text{M}$. This preliminary result, together with the remarkable water interface compatibility makes this material a promising versatile matrix for multiple applications that require contact with aqueous environment such as sensing, heavy metal extraction from water, etc. Some of the mentioned applications are under investigation by our group together with other detection methodologies such as time-resolved fluorescence techniques in order to improve the sensitivity and lower the detection limits.

■ ASSOCIATED CONTENT

📄 Supporting Information

Synthetic procedures, characterization data of LMOG **1**, gelation tests and CCG for the complete set of solvents, FT-IR spectra, SEM images of xerogels, and T_{g} vs concentration plots. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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ABBREVIATIONS

LMOG, low molecular weight organogelator
CCG, critical concentration for gelation

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