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Enantioselective Gel Collapsing: A New Means of Visual Chiral Sensing

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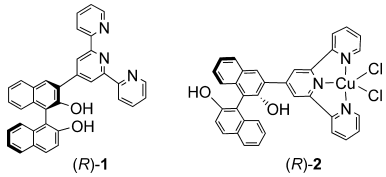
The two most convenient visual detection methods used in classical chemical analysis are color changing and precipitate formation. In recent years, molecular gel formation and collapsing have been shown to be useful in visual sensing because molecular gels are found to be highly responsive materials.[1−4] Many chiral molecules can form gels in various solvents and have exhibited remarkable chiral effects.[5−7] Although external stimuli, such as temperature, pH, and guests, on gels have been extensively investigated, much less research has been conducted on using gels for chiral recognition.[8−12] Herein, we wish to report the first example of enantioselective gel collapsing as a new means of visual chiral sensing.[13] This gel response is compared with the solution fluorescent recognition.

When the 1,1′-bi-2-naphthol (BINOL) and terpyridine conjugate, (*R*)-**1**,[14] were treated with $CuCl_2 \cdot 2H_2O$ (1.2 equiv) followed by concentration and addition of H_2O, the BINOL-terpyridine-Cu(II) complex (*R*)-**2** was obtained as a green solid. The UV spectrum of (*R*)-**2** in $CHCl_3$ gives absorptions at λ_{max} (log ε) = 228 (5.01), 284 (4.16), and 340 (4.58) nm. The long wavelength absorption of (*R*)-**2** at 340 nm was absent in the UV spectrum of (*R*)-**1**, indicating a better conjugated π system of (*R*)-**2** after Cu(II) coordination. The d−d transition of Cu(II) could not be observed in the dilute solution of (*R*)-**2**, but a weak and broad signal around 750 nm was observable in the saturated solution of (*R*)-**2**.



(*R*)-**1** (*R*)-**2**

A sample of (*R*)-**2** at 3.13% (w/v, g/mL) (4.79×10^{-2} M) in $CHCl_3$ was not completely soluble and formed a green suspension. When ultrasound was applied to this suspension for 1 min with a sonicator of 0.40 W/cm^2 and 40 kHz, the sample was then allowed to stand at room temperature for 30 s and an opaque green and unmovable gel was produced (Figure 1). Traditionally, supramolecular gels are prepared by heating a gelator in a specific solution and then cooling the supersaturated solution to room temperature. Ultrasound was previously considered unsuitable for gel formation since it is normally used to cleave the weak noncovalent interactions and break the supramolecular assembly.

In 2005, Naota and Koori demonstrated that sonication can be used to induce changes in molecular structures and intermolecular interactions to generate gels.[15] Quickly following this discovery, a number of reports have appeared on the use of ultrasound to produce molecular gels.[16−21] The acoustic energy of ultrasound is shown to strongly influence molecules and supramolecules, leading to the production of materials that are not accessible by other conventional means.[22]

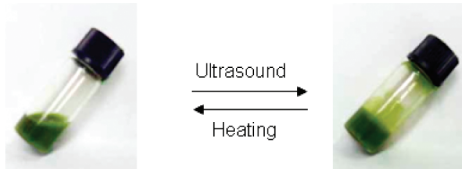


Figure 1. Photographs of the ultrasound induced gelation of (*R*)-**2** and the thermal gel collapsing.

When the ultrasound-induced gel of (*R*)-**2** was heated at 62 °C for 30 min, it collapsed back to the suspension (Figure 1). The critical concentration for the sonication-induced gelation of (*R*)-**2** was found to be 1.72%. Other solvents such as CH_2Cl_2 and CH_3CN could also form a gel with (*R*)-**2** upon sonication. The UV spectrum of the gel generated by sonication in $CHCl_3$ showed no change in the peak shape and position, indicating little structural change upon sonication. At 1.29×10^{-5} M, (*R*)-**2** formed a homogeneous solution in $CHCl_3$ which also showed little change in the UV spectrum after sonication.

To probe the structure of the gel of (*R*)-**2**, X-ray analyses were performed. Slow evaporation of a green solution of (*R*)-**2** in MeOH/acetone led to the formation of the green needle crystals of (*R*)-**2**. A single crystal X-ray analysis shows that each unit cell contains two slightly different molecules of (*R*)-**2**. The dihedral angles of the BINOL units are 70.46° and 71.93° respectively. Each Cu(II) center is five-coordinated with a distorted trigonal bipyrimidal structure. In this structure, the two nitrogen atoms of the side pyridine rings of (*R*)-**2** are located on the axial positions and the central pyridine nitrogen and the two Cl atoms at the equatorial positions, similar to that reported for Cu(terpyridine)Cl_2.[23] The main force for the molecular assembly is probably the $\pi-\pi$ interaction between the terpyridine units as shown in Figure 2a. The pyridine ring 1′ of the middle molecule is stacking with the pyridine ring 3 of the molecule above. The pyridine rings 2′ and 3′ of the middle molecule are stacking with the pyridine rings 1″ and 2″ of the molecule below. There are additional intermolecular interactions through the hydrogen bonds of Cl···H−O in which the Cl···H distance is 2.223 Å and the H−O distance is 0.831 Å (Figure 2b). Figure 2c shows the supramolecular assembly of (*R*)-**2** in the crystal with both the $\pi-\pi$ stacking and the Cl···H−O hydrogen bonds.

The powder X-ray analysis of the xerogel prepared from the air-dried gel of (*R*)-**2** in $CHCl_3$ was conducted and compared with the powder X-ray diffraction pattern of the crystals (Figure 3). For the gel, strong peaks at 2θ = 5.2° (17.43 Å), 11.8° (7.49 Å), 15.7° (5.64 Å), 23.7° (3.75 Å), 24.1° (3.69 Å), and 25.2° (3.53 Å) are observed in the small angle region indicating a significantly ordered structure in the gel. For the single crystal, the strong peak at 2θ = 7.2° (12.27 Å) is consistent with the distance between the two (*R*)-**2** molecules linked by a hydrogen bond, and the strong peak at 2θ =

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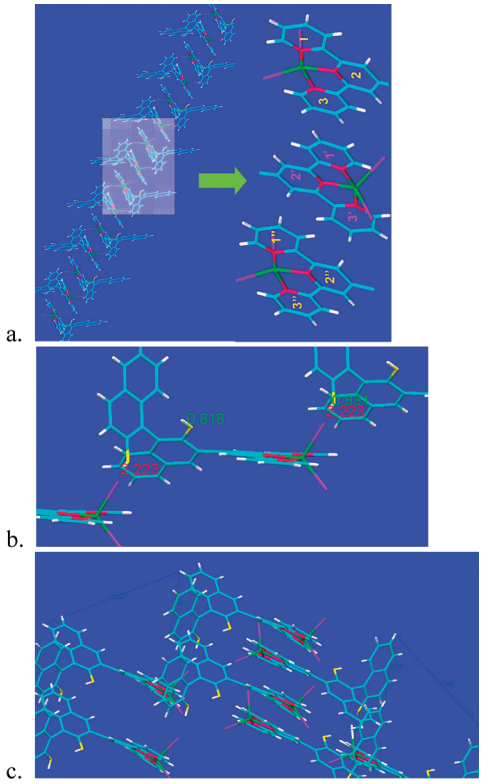

Figure 2. X-ray structure of (*R*)-**2**.

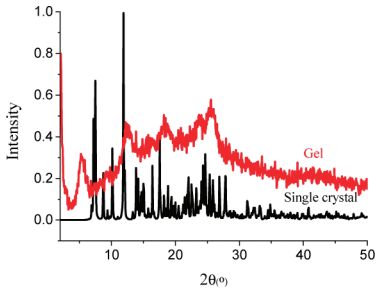

Figure 3. Powder X-ray diffraction patterns of the single crystal and gel of (*R*)-**2**.

7.5° (11.78 Å) is consistent with the distance between the first terpyridine unit and the third terpyridine unit in the three $\pi-\pi$ stacking (*R*)-**2** molecules shown in Figure 2a. In the powder X-ray diffraction pattern of the gel, the peaks at $2\theta = 7.2°$ (12.27 Å) and 7.5° (11.78 Å) of the crystal have disappeared, and a new peak at $2\theta = 5.2°$ (17.43 Å) has appeared indicating enlarged intermolecular distances in the gel. The peaks at $2\theta = 23.7°$ (3.75 Å), 24.1° (3.69 Å), and 25.2° (3.53 Å) for the gel may correspond to the distance between two parallel terpyridine units, indicating that the $\pi-\pi$ stacking of the terpyridine units in the crystal structure may be preserved.

Figure 4 shows the scanning electron microscope (SEM) and transmission electron microscope (TEM) images of (*R*)-**2**. The sample for the SEM image in Figure 4a was prepared from the gel of (*R*)-**2** formed in $CHCl_3$ (3.13%) upon sonication and vacuum-dried for 48 h. The resulting xerogel was shielded with gold and then analyzed. The SEM image shows the formation of a three-dimensional network composed of entangled fibers with a diameter of tens to hundreds of nanometers. The TEM specimen was prepared by gently placing a homogeneous solution of (*R*)-**2** (5.89 mM) in $CHCl_3$ on a surface of the carbon-coated copper grid and

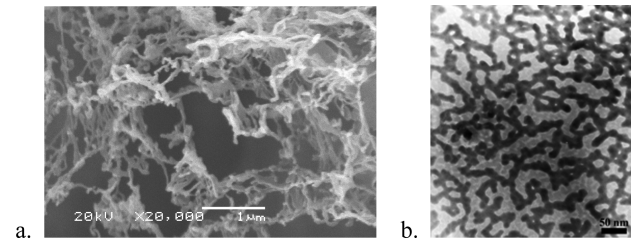

Figure 4. (a) SEM image of xerogel obtained from the gel of (*R*)-**2** in $CHCl_3$, Au shadowing at 45°. (b) TEM image (unstained) of (*R*)-**2** from a $CHCl_3$ solution on carbon-coated copper grid.

then allowing it to dry for 2 min at room temperature. The TEM image in Figure 4b indicates the presence of well-grown distinct fibrillar assemblies with a uniform diameter of 20−30 nm. Thus, sonication probably caused the reorganization of the assemblies of the molecules, leading to the much larger entangled fibers as shown in Figure 4a, to immobilize the solvent.

The responses of the gel of (*R*)-**2** toward the enantiomers of chiral amino alcohols were studied. To a gel of (*R*)-**2** (15 mg) in $CHCl_3$ (0.40 mL) (3.75%), formed by sonication for 1 min, a solution of (*R*)-phenylglycinol (0.10 equiv) in $CHCl_3$ (0.1 mL) was added. When the mixture was sonicated for 2 min, the gel remained stable (Figure 5a). However, when the solution of (*S*)-phenylglycinol was added to the gel of (*R*)-**2** under the same conditions, the gel collapsed (Figure 5b). We found that a 2-fold greater amount of (*R*)-phenylglycinol compared to (*S*)-phenylglycinol was required to cause the gel of (*R*)-**2** to collapse. Compound (*S*)-**2**, the enantiomer of (*R*)-**2**, was also prepared which showed the opposite enantioselective gel collapsing. This confirms the enantioselective nature of the gel response toward the amino alcohol. Similarly, when treated with a $CHCl_3$ solution (0.10 mL) of (*R*)-1-amino-2-propanol (0.10 equiv), the gel of (*R*)-**2** (4.29%) in $CHCl_3$ (0.35 mL) was stable, but the use of (*S*)-1-amino-2-propanol led to gel collapse under the same conditions.

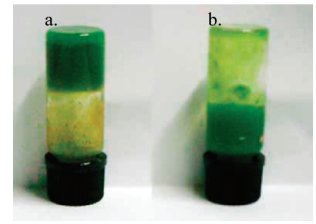

Figure 5. Enantioselective responses of the gel of (*R*)-**2** toward (a) (*R*)-phenylglycinol and (b) (*S*)-phenylglycinol.

Although one report on the enantioselective formation of a molecular gel in the presence of chiral amine guests has recently appeared,[12] there was no report on how a stable molecular gel responds to the enantiomers of a chiral molecule. Figure 5 presents the first example of an enantioselective gel collapsing which provides a new means of visual chiral discrimination.

The chiral recognition of the gel is compared with the fluorescence responses of (*R*)-**2** toward (*R*)- and (*S*)-phenylglycinol in solution. The fluorescence of the BINOL-terpyridine ligand (*R*)-**1** shows a strong emission at $\lambda = 396$ nm in CH_2Cl_2/*n*-hexane (2:3) ($\lambda_{exc} = 289$ nm). This emission is almost completely quenched in the Cu(II) complex (*R*)-**2** (Figure 6). When (*R*)-**2** was treated with an excess amount of (*S*)-phenylglycinol, the emission at 396 nm was greatly enhanced (Figures 6 and 7). This indicates that the amino alcohol might have displaced the Cu(II) ion off the ligand in (*R*)-**2** and restored the emission of (*R*)-**1**. The UV spectroscopic study also supported this hypothesis.

When (*R*)-**2** was treated with (*R*)-phenylglycinol, much weaker fluorescence enhancement was observed. It is proposed that the displacement of the Cu(II) ion in (*R*)-**2** by the chiral amino alcohol is enantioselective with the reaction of (*R*)-**2** with (*S*)-phenylglycinol more favorable than with (*R*)-phenylglycinol.[24] We also found that (*R*)- and (*S*)-phenylglycinol, even in a large excess of (*R*)-**1**, minimally influenced the fluorescence of (*R*)-**1** and showed almost no enantioselectivity. This suggests that the observed enantioselective fluorescence enhancement of (*R*)-**2** in the presence of (*S*)- and (*R*)-phenylglycinol could not be attributed to the interaction of the amino alcohol enantiomers with the free ligand (*R*)-**1** generated after the displacement of the Cu(II) ion of (*R*)-**2**. Significant enantioselective fluorescent enhancements of (*R*)-**2** in the presence of other chiral amino alcohols including prolinol, valinol, phenylalaninol, leucinol, and 1-amino-2-propanol were also observed. These enantioselective fluorescent enhancements are unusual since fluorescent quenching is normally observed when a binaphthyl-based fluorophore is treated with an amine or an amino alcohol.[25−29]

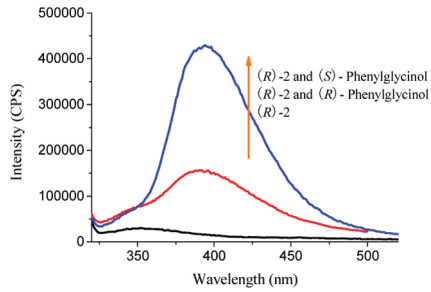

Figure 6. Fluorescence spectra of (*R*)-**2** (5.0×10^{-7} M) in CH_2Cl_2/*n*-hexane (2:3) in the presence of (*R*)- and (*S*)-phenylglycinol (5.0×10^{-4} M) ($\lambda_{exc} = 289$ nm, slits: 2 nm/5 nm).

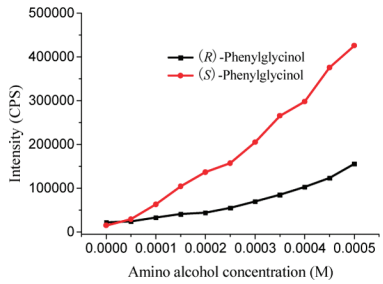

Figure 7. Fluorescence responses of (*R*)-**2** (5.0×10^{-7} M) in CH_2Cl_2/*n*-hexane (2:3) toward (*R*)- and (*S*)-phenylglycinol at $\lambda_{emi} = 396$ nm.

In the fluorescence study, the enantioselectivity can be attributed to the enantioselective displacement of the Cu(II) ion from (*R*)-**2** by the amino alcohol. That is, the reaction of (*R*)-**2** with (*S*)-phenylglycinol might be more favorable than the reaction with (*R*)-phenylglycinol. This reaction occurred with the amino alcohol in a large excess (up to 1000 equiv) of (*R*)-**2** in solution. In the gel study, a very small amount of (*S*)-phenylglycinol [≥0.06 equiv versus (*R*)-**2**] could lead to gel collapse. This indicates that the degree of Cu(II) displacement in the gel by the amino alcohol should be small. The more favorable interaction of (*R*)-**2** with (*S*)-phenylglycinol observed in solution might be greatly amplified in the supramolecular assembly of the gel network, leading to the visually enantioselective response.

In summary, a chiral molecular gel has been prepared by sonication of a BINOL-terpyridine-based Cu(II) complex. Study of the interaction of the gel with chiral amino alcohols led to the discovery of an unprecedented enantioselective gel collapsing. This study demonstrates that the chiral molecular gels are potentially useful for visual chiral discrimination. The chiral Cu(II) complex also exhibits significant enantioselective fluorescent enhancement in the presence of a variety of amino alcohols in solution.

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Supporting Information Available: X-ray data, high resolution mass spectrum, UV and fluorescence spectra, detailed experiments for the gel and fluorescence studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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