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Improving Hg-Triggered Gelation via Structural Modifications

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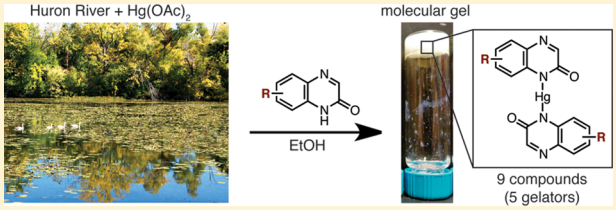
Supporting Information

ABSTRACT: The relationship between chemical structure and gelation ability was examined for a series of nine Hg-containing compounds. Both solid-state properties (dissolution enthalpies/entropies and packing structure) and gel properties (strength, morphology, cation selectivity, and anion tolerance) were examined. Overall, the results reveal a complex relationship between chemical structure and properties. The remediation potential of these Hg-triggered gelations was also investigated, revealing that >98% of the Hg^{2+} in water can be removed through gel formation.



INTRODUCTION

Molecular gels are a class of organic materials that are garnering interest because of their stimulus-responsive behavior.[1−8] As an example, molecular gel-based materials that respond to the presence of metal ions,[9−11] reductants,[12,13] oxidants,[14,15] and enzymes[16−19] have been developed. Despite extensive research in this field, predicting which molecules will form gels remains a major challenge.[20−24] One hypothesis is that the presence of one-dimensional (1D) intermolecular interactions leads to the preferential 1D growth of gel fibers.[25] Based on this hypothesis, we introduced a new approach for discovering gelators that utilizes the Cambridge Structural Database (CSD) to identify molecules that exhibit these 1D interactions in the solid state.[26] In short, the CSD was searched for molecules with intermolecular Hg−arene interactions, from which a $Hg(quinolinone)_2$ compound was identified as the lead structure.[27] Three derivatives of this scaffold were then synthesized and screened for gelation. Excitingly, one of these compounds (**1a**) formed gels in water/organic solvent mixtures. This compound served as a remediation agent, removing >90% of Hg^{2+} ions from water samples through gel formation. There were some limitations, however, including the need for an organic cosolvent, the high concentration of gelator needed to form a gel, and the rapid dissolution of the gel in the presence of Cl^- ions.

With the aim of improving this gel-based material, we now report several alternative structures (Chart 1, **1b**−**5**). Because the intermolecular interactions and solid-state packing of the gel form of **1a** were unknown, several different functional groups were examined. Halogens and extended aromatic systems were chosen because of their demonstrated ability to improve gelation of aromatic peptides in water.[18,28−30] We describe herein the synthesis and gel screening of eight new Hg-containing compounds. Four of these compounds were discovered to form gels, and their gel properties are reported. Comparison of the gelators and nongelators revealed a complex set of solid-state structures that varied based on the preparation method, solvent, and temperature. One of the gelators (**3a**) exhibited marked improvement in Hg^{2+} remediation, removing >99% of Hg^{2+} from water samples at lower concentrations while remaining insensitive to Cl^- ions. Overall, this study highlights the complex interplay between chemical structure, gelation ability, and gel properties.

EXPERIMENTAL METHODS

Gel Screening and Critical Gel Concentration (cgc) Procedure. The cgc was determined by adding a known amount of compounds **1**−**5** (~1−10 mg) to an 8 mL vial containing 1 mL of solvent. The vial was capped, heated to dissolve the solid, and allowed to cool with approximately 20 s of sonication in a water bath (near ambient temperature). If the resulting gel was stable to inversion, then 0.1 mL of solvent was added, and the procedure was repeated until the gel was no longer stable to inversion. If no gel formed initially, then additional $Hg(quinoxalinone)_2$ was added, and the procedure was repeated until the solubility limit was reached.

Procedure for Measuring Equilibrium Solubilities. Compounds **1**−**5** (10 mg × 3 vials per compound) and ~7.5 mL of solvent (EtOH or MeOH) were separately added to 8 mL vials, and the solutions were heated at 45 °C for 7 days. Powder X-ray diffraction (PXRD) analysis was used to identify the solid forms present before and after heating. (Samples were prepared for PXRD by pipetting the mixture onto a microscope slide and allowing the solvent to evaporate prior to analysis.) The solvent was then evaporated from the vials by heating at 45 °C for 5 h with the caps removed. PXRD analysis was again performed to verify that the solid form for each compound remained unchanged after evaporation. New solvent (~6−7 mL of EtOH or MeOH) was added to the vials, and the mixtures were equilibrated for 48 h at 25, 30, 40, and 50 °C. Aliquots (200 μL) were removed at each temperature and diluted with a known amount of solvent (~3−4 mL). The solution concentration was determined using UV−vis spectroscopy and a calibration curve. To minimize sampling error, the solubility was determined by averaging the results of three aliquots from each vial (nine aliquots total) at each temperature. van't Hoff plots [$\ln(x)$ versus $1/T$, where x is the mole fraction solubility]

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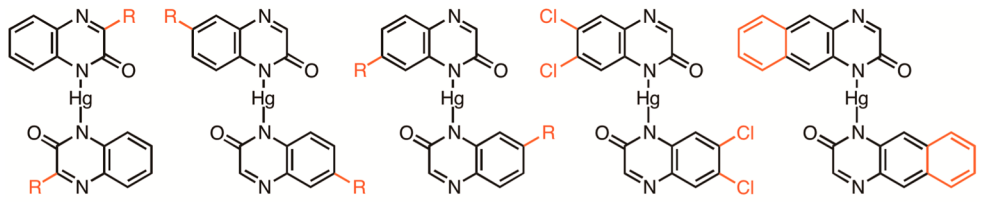
Chart 1



1a R = H; **1b** R = CH_3; **2a** R = Br; **2b** R = Cl; **2c** R = F; **3a** R = Br; **3b** R = Cl; **4**; **5**

were employed to determine the dissolution enthalpies (ΔH_{diss}) and entropies (ΔS_{diss}) using the equation

$$\ln(x) = -\frac{\Delta H_{diss}}{RT} + \frac{\Delta S_{diss}}{R} \quad (1)$$

The error bars reported at each point on the van't Hoff plots were calculated as the relative error ($\Delta x/x$).

Representative Procedure for Hg^{2+} Remediation. A gel of **1a** was prepared by mixing quinoxalin-2(1H)-one (9.4 mg, 0.064 mmol) and $Hg(OAc)_2$ (9.6 mg, 0.030 mmol) in MeOH/H_2O (1 mL, 70/30 v/v). A spatula was used to gently compress the gel and release the entrapped solvent (see Figure S55 in SI). An aliquot (~20 μL) was taken, and the solvent was removed in vacuo. Then, 2.8 mL of HNO_3/H_2O (5/95 v/v) and a yttrium standard (0.140 μL of a 100 ppm stock solution) were added to the vial. The solutions were diluted to 14 mL with deionized H_2O. Inductively coupled plasma-optical emission spectroscopy (ICP-OES) measurements were taken on a Perkin-Elmer Optima 2000 DV spectrometer. The detection limit for Hg^{2+}, analyzed at a wavelength of 194.167 nm, was approximately 10 ppb. Yttrium was used as an internal standard and detected at a wavelength of 371.029 nm. To minimize sampling error, the experiment was repeated three times for each gel, and each sample was analyzed by ICP-OES in triplicate.

RESULTS AND DISCUSSION

Synthesis and Gel Screening. Nine mercury-containing compounds were synthesized and screened for gelation [Chart 1 and Supporting Information (SI)]. Most of the quinoxalinone ligands were synthesized in one step by condensation of a commercially available aryl diamine and glyoxylic or pyruvic acid.[31] Subsequent reaction with $Hg(OAc)_2$ generated the target compounds in moderate yields.[27] Full characterization data for these compounds can be found in the SI. Compounds **1**–**5** were screened for gel formation using the heat/cool method with sonication during the cooling phase. Initial gel screening revealed that five compounds (**1a**, **2b**, **2c**, **3a**, and **3b**) formed gels in at least one solvent system (Table 1 and Table S1 in the SI). Gelation was found to be highly sensitive to both the solvent composition and structure. As an example, whereas gelator **3b** formed gels in MeOH, EtOH, and EtOH/HOAc, its regioisomer, **2b**, formed gels in only EtOH/HOAc. Similarly, compound **3a** formed gels in EtOH and EtOH/HOAc, whereas its regioisomer, **2a**, did not form gels in any of the solvents examined. These results lead to the conclusion that the gel formation is largely dictated by the position and nature of the substituents, rather than being dominated by the quinoxalinone framework.[32,33]

Table 1. Critical Gel Concentrations (cgc, mM) in Selected Solvents

gelator	MeOH	EtOH	EtOH/HOAc[a]
1a	30 ± 1	precip	precip
2b	precip	precip	3.5 ± 0.4
2c	precip	15 ± 0	precip.
3a	precip	10.2 ± 0.3	5.0 ± 0.0
3b	3.5 ± 0.1	3.9 ± 0.2	7.1 ± 0.3

[a]10 μL of HOAc in 1 mL of EtOH.

Solubility and Dissolution Parameters. We previously reported that gelators exhibit (on average) higher dissolution enthalpies (ΔH_{diss}) and entropies (ΔS_{diss}) than nongelators.[23,24] This result suggests that gelators have stronger solid-state interactions and/or weaker solvent–solute interactions than nongelators. To determine whether this correlation is generally applicable, we initiated solubility studies on compounds **1**–**5**. Because dissolution parameters are solvent-dependent, a single solvent system wherein all gelators form stable gels is desired. As is evident in Table 1, our initial gel screening did not reveal any common solvents for all five gelators. As a result, we identified potential alternative solvents using a program centered on the Hansen solubility parameters (HSPiP).[34] Although these parameters are typically used to identify solvents that will solubilize compounds, several groups have successfully extended this type of analysis to gel formation.[20−22,35−38] Compound **1a** was selected for this analysis based on its facile synthesis from commercially available reagents. On the basis of the solubility characteristics of **1a** in eight different solvents, the HSPiP program generated a list of approximately 1200 potential solvents. Solvents with a "relative energy difference"[39] of less than or equal to 1 were selected for further exploration, generating a more manageable list of approximately 300 solvents. This list was further narrowed to nine solvents by taking into account boiling points, the nature of functional groups, and accessibility (Table S2 in SI). Some representative examples include 2-pentanol, 3-methoxypropanol, and 2,2,2-trifluoroethanol. Of these, compound **1a** was only able to form gels in 2,2,2-trifluoroethanol, and further screening revealed that none of other compounds formed gels in this solvent (Table S1 in SI). As a consequence, we were still unable to identify any solvent systems wherein more than three of the five compounds formed gels. Nevertheless, we reasoned that comparisons across solvents would prove valuable and proceeded with variable-temperature solubility measurements for **1**–**5** in both MeOH and EtOH.

In our previous work, the solubility measurements were performed on the bulk solid obtained directly from synthesis. Powder X-ray diffraction (PXRD) analysis was used to determine whether the bulk solid was representative of the gel form. If the solid-state packing was different between these two forms, the equilibrium solubilities were not measured.[23,24] For all gelators described herein, the solid-state packing in the bulk solid did not match that in the gel form (Figures S24–S32 in SI).

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Further PXRD analysis revealed that all nine compounds underwent a solid−solid transformation (bulk form → new form) in MeOH and that some did in EtOH as well. As a representative example, the complex polymorphism exhibited by compound **1a** is highlighted in Figure 1. We observed a total

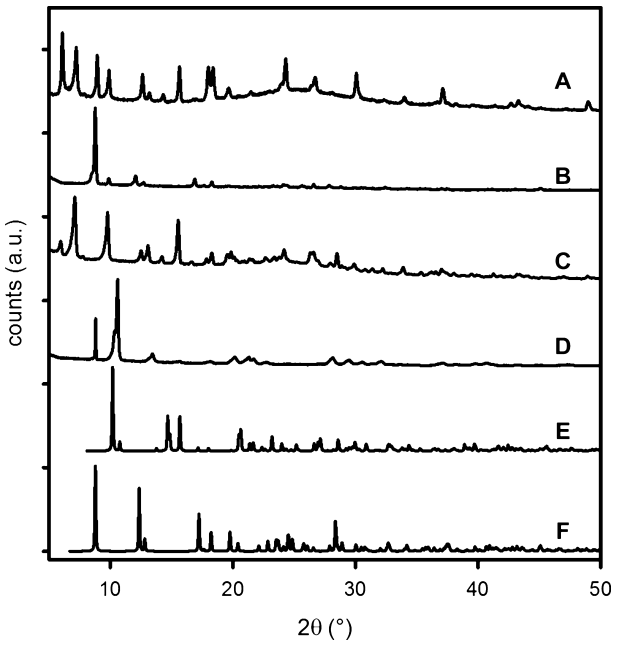

Figure 1. PXRD patterns for gelator **1a** under the following conditions: (A) gel form in MeOH, (B) solid form after heating in EtOH, (C) solid form after heating in MeOH, (D) bulk form isolated from synthesis, (E) simulated pattern from crystal grown from MeOH/H_2O, (F) simulated pattern from crystal grown from DMSO/H_2O.

of five different forms, including the gel form, bulk form, heated-in-EtOH form, and two single-crystal structures (see also Figures S22−S23 in SI). We suspected that some of these forms are solvates. Differential scanning calorimetry studies confirmed that there are no obvious transitions that interconvert these forms in the solid state (Figures S33−35 in SI). In addition, thermogravimetric analysis revealed an initial solvent loss upon heating for some (but not all) of the gelator forms examined, which suggests that these compounds exhibit both solvates and polymorphs (Figures S56−S59 in SI). Overall, of the >20 different solid forms observed for compounds **1**−**5** in these experiments, only one matched the gel form (i.e., heated form of **1a** in MeOH). Because the extent to which these differences in the solid-state structure might influence the relative discrimination of gelators and nongelators was unclear, we proceeded with the variable-temperature solubility measurements. Note that the most stable (heated) form was used in the solubility measurements. The results of these solubility studies are highlighted in Figure 2.

Overall, the conclusions are tenuous given that (i) the solid forms do not exhibit the same molecular packing as the gel form and (ii) the data set for each solvent system is limited. Nevertheless, useful comparisons can be made. For example, for all nine compounds, the ΔH_{diss} value is ∼5−10 kcal/mol higher in MeOH than in EtOH. This result can be attributed to the different solid forms, which would reflect a change in the solid-state interactions, or to the different solvent properties (e.g., hydrophobicity), which would reflect a change in the solvent−solute interactions. Overall, these studies revealed that comparisons among structurally similar gelators and nongelators can be challenging if the compounds do not all gel in the same solvent system and are polymorphic under the conditions used in the analysis.

Gel Properties. The critical gel concentrations ranged from 3.5 to 30 mM, depending on both chemical structure and solvent composition (Table 1). For example, whereas the addition of HOAc lowered the cgc of compound **3a**, it increased the cgc of compound **3b**. All gels displayed characteristic viscoelastic behavior, with a ratio between the elastic and storage moduli (G'/G'') of greater than 10 (Figure 3 and Figures S42−S45 in SI). In addition, the gels were robust, exhibiting a breaking stress near 100 Pa. These values are similar to those of other metal-containing molecular gelators.[9,12] Scanning electron microscopy revealed a dense network of fibers for all gels, although the fiber diameters varied among the gelators (0.1−1.5 μm, Figure 3 and Figures S46−S50 in SI).

Hg^{2+} Remediation. Stimulus-responsive gelation represents an appealing platform for both detecting environmental contaminants and removing them. In 2010, we reported that **1a** can be used to effectively remove >90% of Hg^{2+} ions from an aqueous solution through gelation.[26] However, its practical utility was limited by its relatively high cgc and ready dissolution upon addition of Cl^- ions. As a consequence, we investigated the remediation potential of the four new gelators: **1a**, **2c**, **3a** and **3b**.[40] Gel formation was instantaneously observed when Hg-contaminated water was added to a MeOH solution containing each of the quinoxalinones at the appropriate concentration (Figure 4 and Figure S51 in SI). The gelators exhibited similarly high remediation abilities (>98% Hg^{2+} removed, Table S6 in SI). The improved performance for **1a**, compared to our earlier work,[26] is due to the superstoichiometric amounts of quinoxalinone used herein. Gel formation was found to be remarkably selective for Hg^{2+} over other metal ions (Figure S51 in SI), possibly because of the linear geometries of these complexes, which would facilitate 1D intermolecular interactions.

The chloride-ion tolerance of the gels was also examined because we previously reported that gels of **1a** dissolved upon addition of NBu_4Cl,[26] limiting its practical application. Remarkably, gels of **3a** were completely resistant to chloride treatment and remained stable for months (Figure S52 in SI). This stability to Cl^- ions was not observed with the other gelators. We hypothesized that these results reflect the relative stabilities of the various complexes [$HgCl_2$ versus Hg(quinoxalinone)$_2$] rather than a kinetic phenomenon. To test this hypothesis, we performed a series of ligand-displacement experiments using 7-bromoquinoxalin-2(1H)-one (from **3a**) and the 6-fluoroquinoxalin-2(1H)-one (from **2c**) and monitored the reactions using ^{19}F NMR spectroscopy (Figures S18−S20 in SI). These studies revealed that rapid exchange of the quinoxalinone ligands occurred during mixing. When the two quinoxalinones were present in equal concentrations and were competing for a substoichiometric amount of Hg^{2+} ions, complex **3a** formed preferentially over complex **2c**, indicating that the relative binding affinities of the two quinoxalinones are different.[41] This stronger binding affinity of the 7-bromoquinoxalin-2(1H)-one might explain why complex **3a** is more resistant than **2c** to ligand exchange by Cl^- ions.

To probe the robustness of this sensing platform, environmentally relevant water sources (bottled water, tap water, and Huron River water) were also examined. Because the Hg^{2+}

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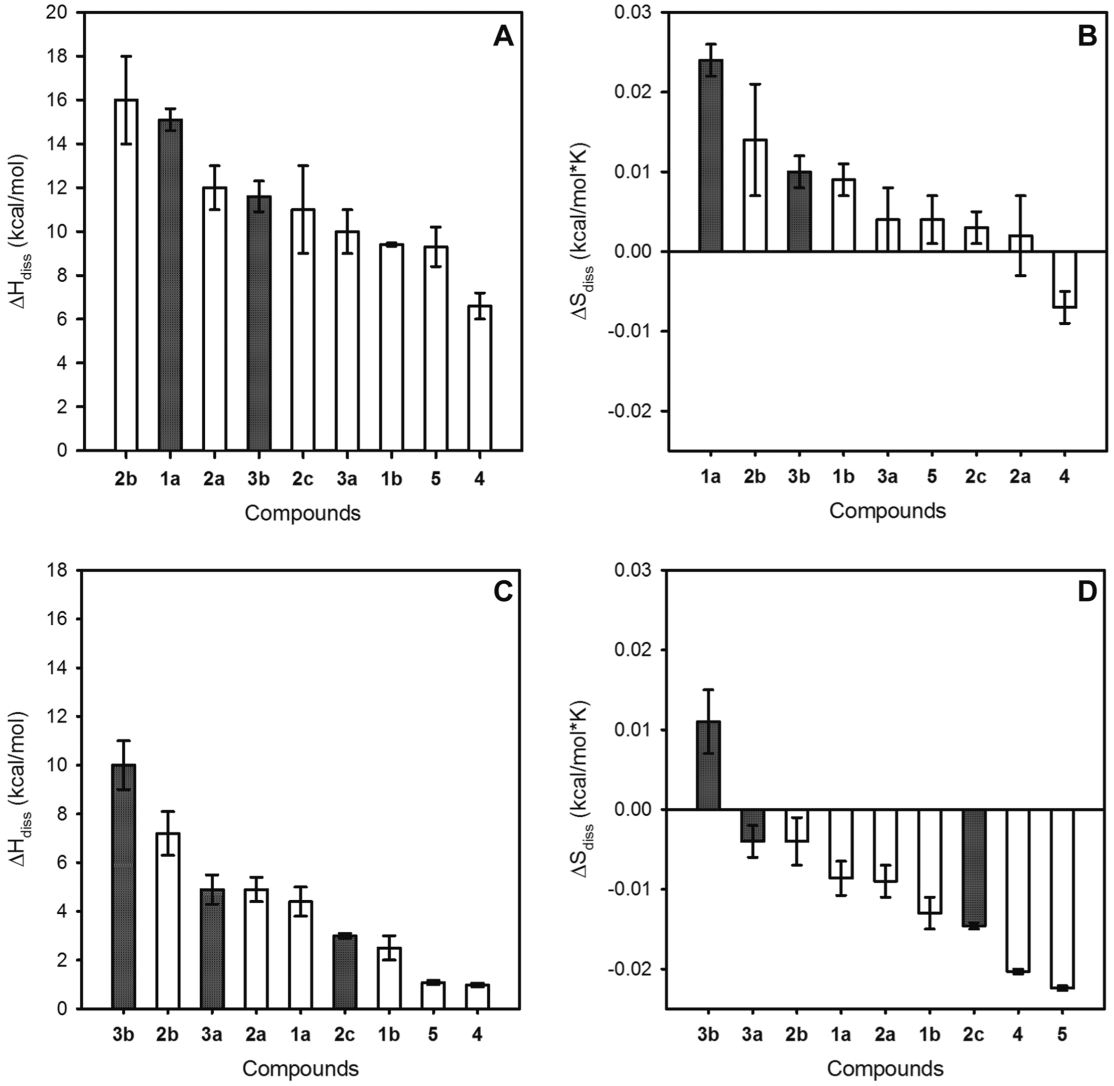

Figure 2. Plots of dissolution (A,C) enthalpy (ΔH_{diss}) and (B,D) entropy (ΔS_{diss}) versus compound number for **1**−**5** in (A,B) MeOH and (C,D) EtOH. Gray shading denotes gelators.

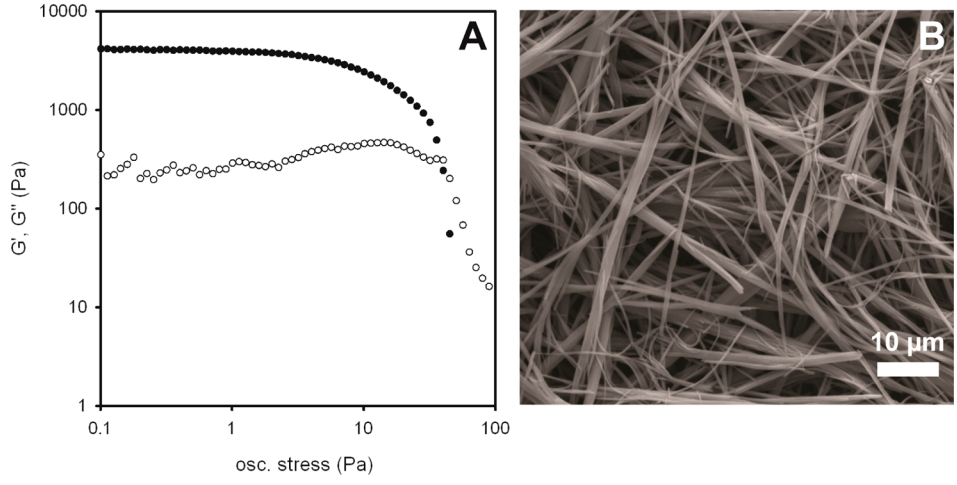

Figure 3. (A) Representative oscillating stress sweep for gelator **3a** in EtOH (15 mM). (B) Representative scanning electron micrograph for gelator **3a** in EtOH/HOAc (12.3 mM).

concentrations in these natural samples are low, $Hg(OAc)_2$ was added to the water prior to analysis. Gelation of **3a** was observed when these water samples were added to an EtOH solution containing 7-bromoquinoxalin-2(1H)-one with brief

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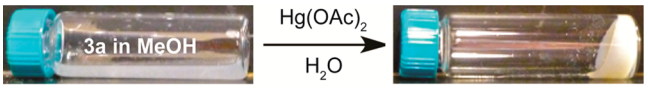

Figure 4. Gelation observed when Hg^{2+}-contaminated water (0.2 mL, 48 mM) is added to a MeOH solution containing 7-bromoquinoxalin-2(1H)-one (0.8 mL, 20 mM).

sonication. A control experiment confirmed that no gels formed when unaltered water samples [i.e., no added $Hg(OAc)_2$] were used, consistent with Hg-triggered gel formation (Figure 5).

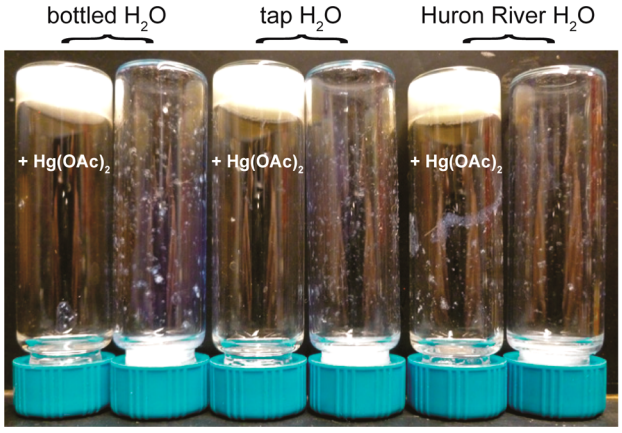

Figure 5. Gel formation (with **3a** in EtOH) observed when bottled water, tap water, and Huron River water containing $Hg(OAc)_2$ are added.

CONCLUSIONS

The synthesis and evaluation of nine Hg-containing compounds was described. Five of these compounds formed gels in organic solvent/water systems. Comparison of the gelators and nongelators based on dissolution enthalpies and entropies was complicated by the lack of a common solvent system for gelation and the large variety of accessible solid forms. The gels were all composed of dense networks of fibers, although the fiber diameters varied among the gelators. Despite these differences, the gelators all exhibited similar rheological properties near their critical gel concentrations. We also demonstrated that these Hg-triggered gelations can effectively remove >98% of the Hg^{2+} in aqueous solutions and are able to occur in complex samples (e.g., river water), suggesting that a promising application of these stimulus-responsive materials might be in environmental remediation.

ASSOCIATED CONTENT

Supporting Information

Experimental details, synthetic procedures, spectroscopic data, powder X-ray diffraction patterns, differential scanning calorimetry data, gel screening, solubility data, rheological data, microscopy images, gelation experiments, Hg^{2+} remediation data, thermogravimetric analysis, and CIF files. 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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(39) Relative energy difference (RED) refers to the distance from the center of the solvent "sphere" divided by the radius (see SI).
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(41) We note that the "mixed" complex, containing both ligands, is formed in the highest concentration (see SI).