# Streamlined approach to a new gelator: inspiration from solid-state interactions for a mercury-induced gelation†

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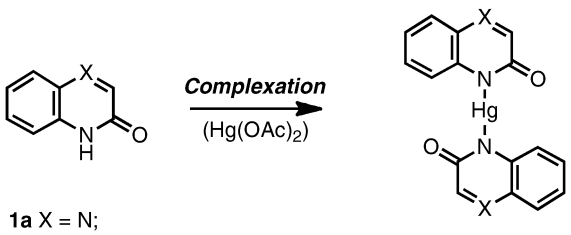
**A new gelator was discovered by identifying molecular scaffolds exhibiting 1D intermolecular interactions in the solid-state and synthesizing derivatives. Gelation can be triggered by adding $Hg(OAc)_2$ to a precursor molecule. The *in situ* gelation is selective for $Hg^{2+}$ over other metals.**

Molecular gels are a class of organic materials that exhibit solid-like rheological properties despite being mostly composed of liquid.[1] These properties originate from their continuous microscopic structure that is formed by non-covalent self-assembly of small molecules. Molecular gels are being widely investigated for diverse applications such as sensing,[2,3] regenerative medicine,[4] and environmental remediation.[5] Despite intense research on these materials, the relationship between molecular structure and gelation ability is still poorly understood.[6] As a result, designing new gelators remains a significant challenge.

To date, the most successful strategy for creating new gelators has been to modify known gelator scaffolds. In contrast, several *de novo* design strategies have been proposed by us[2] and others.[7] These strategies are based on an early hypothesis by Hanabusa *et al.*[8] in which it is suggested that an important criterion for developing gelators is to have "intermolecular interactions for building up macromolecule-like aggregates." The implication is that unidirectional (or 1D) interactions should promote 1D self-assembly, leading to the fiber-like morphologies typically observed in molecular gels. This hypothesis has been supported in several cases where predominant 1D interactions observed in gelator single-crystal X-ray structures have been shown to be maintained in the gel fibers by powder X-ray diffraction.[9] Yet predicting which molecules will exhibit these interactions remains a significant challenge. We believe that the discovery of new gelators can be streamlined by using the Cambridge Structural Database (CSD)[10] to identify molecular scaffolds which show predominant 1D intermolecular interactions and are easily synthetically modified. As evidence, we describe herein the successful discovery of a new gelator using this approach.

We postulated that $Hg^{2+}$ ions could promote 1D self-assembly and gelation of an aromatic molecule *via* cation–π interactions. The CSD was searched for molecules that exhibit this interaction and the search led to compound **2c**, reported by Goodgame and co-workers in 1992.[11] The solid-state packing of planar **2c** exhibited 1D aryl–Hg–aryl (π–cation–π) interactions. Based on these predominant 1D interactions, we predicted that either this $Hg^{2+}$ complex or structurally related derivatives may be gelators. In addition, because these cation–π interactions are only available when $Hg^{2+}$ is present, we predicted that the precursors (**1**) would not form gels under the same conditions as **2**.[12–14]




**1a** X = N;
**1b** X = CH;
**1c** X = C-$CH_3$;

**2a-c**

Complexes **2a–c** were prepared in high yields (> 80%) from commercially available quinoxalinone **1a** or quinolinones **1b–c** and $Hg(OAc)_2$ (ESI†).[11] Complex **2a** formed gels in several different MeOH/$H_2O$ mixtures. On the other hand, complexes **2b** and **2c** did not form gels in any of the organic solvent/water mixtures examined. The critical gel concentration (cgc) of **2a** is 25 mM (1.6 wt%) in 90/10 MeOH/$H_2O$ at 25 °C. Gelator **2a** did not form stable gels in mixtures of water with any other organic solvent tested (*e.g.*, DMSO, DMF, acetone, or THF). Although **1a** did form gels in MeOH/$H_2O$, the cgc was much higher, suggesting that the $Hg^{2+}$ ion is playing an important role in the gelation of **2a** (Table 1).

Gelation can be triggered by adding $Hg(OAc)_2$ to **1a** *in situ*. For example, adding an aqueous solution of $Hg(OAc)_2$ to a hot solution of **1a** in MeOH led to a stable gel within 10 min (Fig. 1). A control experiment confirmed that simply adding an equivalent volume of water to **1a** led to precipitation. Comparing the cgc for gels prepared *in situ versus* those formed with isolated **2a** indicates that the released HOAc has a negligible effect (Table 1). The metal-ion induced gelation appears to be specific to $Hg^{2+}$; independently adding aqueous

**Table 1** Critical gel concentrations for **1a** and **2a**[a]

| MeOH/$H_2O$ (v/v) | **1a**/mM | **2a** isolated/mM | **2a** *in situ*/mM |
|---|---|---|---|
| 90/10 | 191 ± 6 | 25 ± 1 | 23 ± 2 |
| 80/20 | 162 ± 4 | 24 ± 2 | 24 ± 0 |
| 70/30 | 155 ± 4 | 26 ± 0 | 22 ± 2 |
| 60/40 | — | — | 21 ± 0 |

[a] Reported cgcs represent an average of three runs (ESI†).

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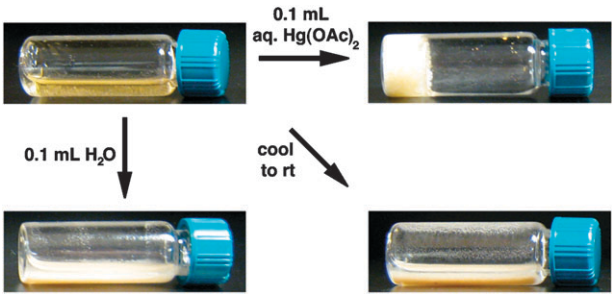


**Fig. 1** Adding an aqueous solution of $Hg(OAc)_2$ to **1a** in hot MeOH (upper left) leads to gel formation (upper right). Control experiments show that simply adding an equivalent volume of $H_2O$ (lower left) or cooling to rt (lower right) results in precipitation.

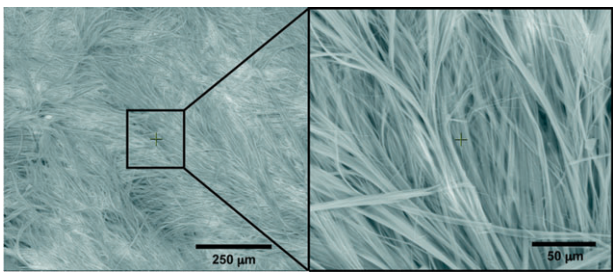


**Fig. 2** Scanning electron micrograph of the *in situ* gel of **2a** (24 mM) in 90/10 MeOH/$H_2O$.

solutions containing $Co(OAc)_2$, $Ni(OAc)_2$, $Cd(OAc)_2$, $Ba(OAc)_2$, $Cu(OAc)_2$, $Zn(OAc)_2$, or AgOAc to **1a** in MeOH led to precipitation (ESI†). Though this Hg-selective gelation could function as a sensor, the sensitivity is too low to be practical (~4000 ppm).

The gel microstructure consists of bundles of high-aspect-ratio fibers as shown *via* scanning electron microscopy (Fig. 2). Rheological measurements confirmed that **2a** forms a visco-elastic gel-like material (ESI†). X-Ray quality single-crystals of **2a** were obtained from DMSO/$H_2O$ solutions. Surprisingly, X-ray diffraction analysis revealed that the predominant intermolecular interactions were π-stacking between the quinoxalinones (3.54 Å) and not the cation–π interactions as anticipated (Fig. 3). An intermolecular carbonyl–Hg–carbonyl interaction (2.88 Å) was also observed. Powder X-ray diffraction studies revealed that the solid-state packing in the single-crystal (obtained from DMSO/$H_2O$) is different than the gel fibers (in MeOH/$H_2O$, see ESI†). Thus, cation–π interactions may still be involved in the $Hg^{2+}$-induced gelation.

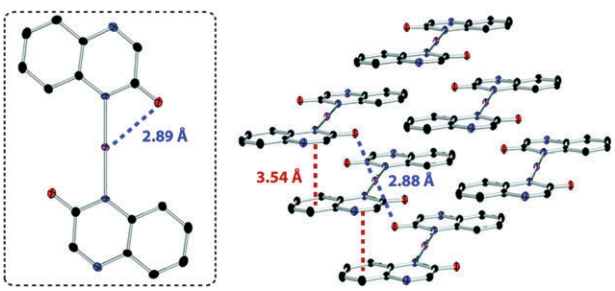


**Fig. 3** Single crystal X-ray structure for **2a**. H-atoms were omitted for clarity.

The role of the counterion was probed by adding an aqueous solution of $HgCl_2$ to **1a** in MeOH. Single-crystal X-ray diffraction analysis on the product revealed that $HgCl_2$ was ligated by two quinoxalinones (ESI†). The selective formation of this complex can be understood based on the stronger binding strength of $Cl^-$ than $^-OAc$ to cationic mercury.[15] A screen of solvent mixtures and concentrations revealed that this complex does not form gels under any conditions tested. Interestingly, adding 1 equiv. $Bu_4NCl$ to a gel of **2a** resulted in complete breakdown of the gel network (ESI†). Such anion-dependent gelations have been observed with other metal complexes.[16,17]

Because molecular gels are mostly composed of liquid, these materials can be utilized to extract pollutants into the solid-phase and a subsequent filtration can recover the liquid.[18] Inductively coupled plasma-optical emission spectroscopy was used to determine whether $Hg^{2+}$ can be effectively removed from aqueous solutions with this *in situ* gelation. Mercury ions are highly toxic, persistent pollutants in several water sources[19] and methods for effectively removing mercury are still needed.[20] Indeed, an impressive reduction in mercury was observed (ESI†). For example, a 3800 ppm $Hg^{2+}$-contaminated water sample was used to form a gel *in situ*. ICP-OES analysis revealed that 289 ppm $Hg^{2+}$ remained in solution, suggesting that this gel can effectively remove significant quantities of mercury from contaminated water sources.

In summary, a new gelator was discovered *via* a straightforward method which involves identifying molecular scaffolds that show predominant 1D intermolecular interactions in the solid-state, synthesizing derivatives, and testing for gelation ability. Importantly, this approach should prove general for a variety of intermolecular interactions and greatly accelerate the discovery of new classes of gelators. Our current efforts are focused on determining the generality of this method.

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