A resilient and luminescent stimuli-responsive hydrogel from a heterotopic 1,8-naphthalimide-derived ligand†

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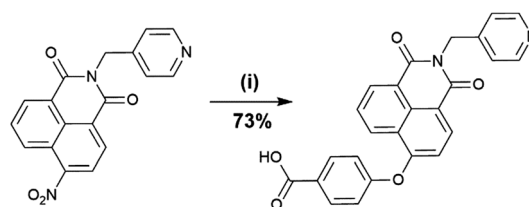
A heterotopic naphthalimide ligand N-(4-picolyl)-4-(carboxyphenoxy)-1,8-naphthalimide HL is utilised for the formation of self-assembled soft materials. In the presence of K^+ ions, L^- forms a robust photoluminescent hydrogel 1 which is reversible under thermal, mechanical or chemical stimuli.

The preparation of functional supramolecular constructs is an area of significant interest in the materials science community, and as the field continues to mature, a prevalent focus for such materials is now the incorporation of stimuli-responsive properties for specific applications.[1] Colorimetric and/or fluorimetric responses to chemical changes in the local environment have been widely harnessed as sensors for ions, changes in pH, vapours, and tests for the presence of biological macro-molecules,[2] while externally addressable rheological properties are a key aspect of controlled drug release from soft materials, particularly gels.[3] Although many fascinating examples of low molecular weight gelators (LMWGs) are known with organic solvent systems (organogels),[4] great interest exists in the pre-paration of new hydrogelators for applications in aqueous media, particularly for biomedical applications.[5] To date, the vast majority of reported LMWGs used in the formation of supramolecular hydrogels contain hydrogen-bonding groups, with the self-assembly process and gel–sol interactions governed by these forces, although often in unpredictable ways.[6] These primary interactions are often supported by π–π stacking inter-actions, as is generally the case in 1,3,5-benzenetricarboxamide derivatives.[7] Although gelation can be induced through other interactions including halogen bonding and metal coordination,[8] small molecule hydro-gelators with no hydrogen bond donors remain challenging to realise.

The 1,8-naphthalimide backbone is an attractive building block for a range of supramolecular assemblies, and has been widely employed in the construction of many organic and metal–organic motifs.[9] As well as the ease of functionalisation of 1,8-naphthalimide derivatives providing diverse libraries of derivatives, the π-conjugation of the backbone leads to structure-directing π–π interactions useful as synthons in metallo-supramolecular architectures.[10] Although 4-amino-1,8-naphthalimides are popular as fluorescent probes, the related 4-oxo-1,8-naphthalimide fluorophores have received far less attention. Following the synthesis and spectroscopic studies carried out by Thilagar and co-workers,[11] only one previous report has detailed the structural and coordination chemistry of such species,[12] focusing on symmetrically-substituted 4-oxonaphthalimide ligands in coordination polymer systems. Here we report the synthesis of a new hetero-ditopic ligand N-(4-pyridyl)-4-(4′-carboxyphenoxy)-1,8-naphthalimide **HL**, and study its propensity to form responsive supramolecular materials.

The ligand **HL** (Scheme 1) was prepared based on our previously reported methodology for the dicarboxylate and dicarbonitrile equivalents.[12] The ligand displays modest photo-luminescence in DMSO solution ($\Phi \sim 0.02$) with emission maximum at 440 nm (λ_{ex} = 366 nm, Fig. S13, ESI†), comparable

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Scheme 1 Synthesis and structure of the ligand **HL**. *Reagents and conditions*: (i) 4-hydroxybenzoic acid, K₂CO₃, DMSO, 120 °C.

to the previously reported dicarboxylate ligand. We briefly examined the interaction of **HL** with d^{10} metal ions; after screening a range of conditions, single crystals of a Cd^{II} complex poly-[Cd**L**$_2$] were isolated and characterised, but this phase was not sufficiently robust on evacuation to allow a thorough study into stimuli-responsive behaviour beyond a solvent-induced phase change. These data are presented as supplementary information (Fig. S1 and S2, ESI†).

The properties of **HL** as a precursor for the generation of self-assembled soft materials were examined following the observation of hydrogel formation during the initial synthesis of **HL**; quenching the reaction mixture directly with water led to thickening of the mixture and the separation of a viscous brown gel. Subsequently, the product was isolated by quenching the reaction with methanol/HOAc to avoid gelation and afford a pure solid. Gel **1** could then be prepared by dispersing **HL** in water and combining with potassium carbonate solution with heating (ESI†). On cooling to room temperature, the pale yellow solution hardened into a robust gel, **1**, within several minutes. As shown in Fig. 1, a monolith of gel **1** *ca.* 1 cm in diameter (10 mg mL^{-1} **HL**, 6 eq. K$_2$CO$_3$, total 3.3 wt%) is sufficiently robust to be handled and manipulated in air, retains its shape under gentle mechanical stress, and is semi-transparent. After coating the gel onto a silicon support and drying under dynamic vacuum to the xerogel, scanning electron microscopy (SEM) revealed a densely packed fibrous morphology with thick and branching fibrils interspersed with crystalline potassium carbonate/bicarbonate by-product (Fig. 1d). The gel is photoluminescent, with an emission maximum at 470 nm (λ_{ex} = 366 nm), which is marginally red-shifted compared to the free ligand in DMSO solution. The blue/green emission of the gel is sufficiently intense to be visualised by the naked eye under UV irradiation (Fig. 1c).

The conditions leading to gel formation were probed to ascertain the influence of K$_2$CO$_3$: **HL** ratio as well as the critical gelator concentration (CGC). Indefinite resistance to inversion was observed at **L** concentrations as low as 2.5 mg mL^{-1} when prepared using 6 equivalents of K$_2$CO$_3$, or 5 mg mL^{-1} when

Table 1 Summary of the physical properties of hydrogels derived from **HL**:K$_2$CO$_3$

Loading HL (mg mL^{-1})	K$_2$CO$_3$ (eq.)	Residual mass (%)	T_m (°C)
10	6	3.3	81(3)
5	1.5	0.9	47(4)
2.5	6	1.3	38(3)

prepared using the minimum possible quantity of potassium carbonate required to achieve a homogenous solution (1.5 eq.). The thermal stability of gels prepared at various concentrations and **HL** : K$_2$CO$_3$ ratios were measured using the bead drop method (Table 1),[13] and show a decrease in thermal stability with decreasing **HL** loading. Each gel could be completely converted to the solution phase by heating to 100 °C, and then almost immediately re-set to its gel form on cooling to room temperature. For the subsequent tests, gel **1** was prepared at a concentration of 10 mg **HL** per mL with 6 equivalents of potassium carbonate; thermogravimetric analysis of this gel revealed a residual mass of 3.3% at 150 °C.

Rheological studies were used to quantitatively probe the mechanical properties of gel **1**. Strain amplitude data show a solid-like behaviour at low strain amplitudes, with the storage modulus (G') plateau at around 30 Pa which is an order of magnitude larger than the loss modulus in this regime (Fig. 2). The intersection point, which corresponds to yielding and flow, occurs at strain amplitude γ = 39%. A frequency sweep experiment shows that the values of G' and G'' are essentially invariant across the entire scan range (Fig. S4, ESI†), while a recovery test, at alternating strain amplitudes of 0.1 and 300%, shows rapid recovery to the original values of G' and G'' after shearing, and over multiple cycles.

The two-component solid fraction of gel **1** was also probed as a means for chemical reversibility of the gelation process. **HL** can be dissolved in water with no thickening or gel formation by deprotonating with tetrabutylammonium hydroxide, with gelation then induced by the addition of potassium chloride (2 eq. *cf.* **HL**). Similarly, no gelation occurs between **HL** and potassium carbonate when 18-crown-6 (2 eq. *cf.* **HL**) is added to the precursor solution, and gelation can then be induced by the subsequent addition of a further 2 equivalents of potassium chloride. The need for free potassium ions to form and maintain the gel is consistent with the observations by Feringa, Browne and co-workers on the relationship between stability and ionic strength in a series of cyclohexanetriamide gels, ascribed to the reduction of carboxylate-carboxylate repulsion.[14] Interestingly, no gelation was observed under any experimental conditions when employing the 3-picolyl-substituted isomer of **HL**, implying an additional steric influence consistent with coordination through the pyridyl group. The gelator **L** is especially unusual as a low molecular weight hydrogelator containing no classical hydrogen bond donors, implicating potassium-carboxylate coordination and π–π interactions as the most substantial intermolecular forces.

As well as a mechanistic probe, the relationship between gelation and K$^+$ concentration provides a chemical trigger for
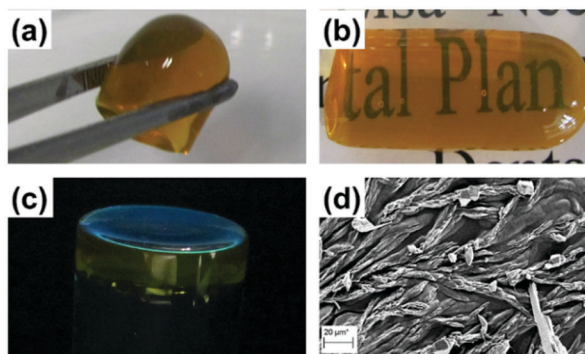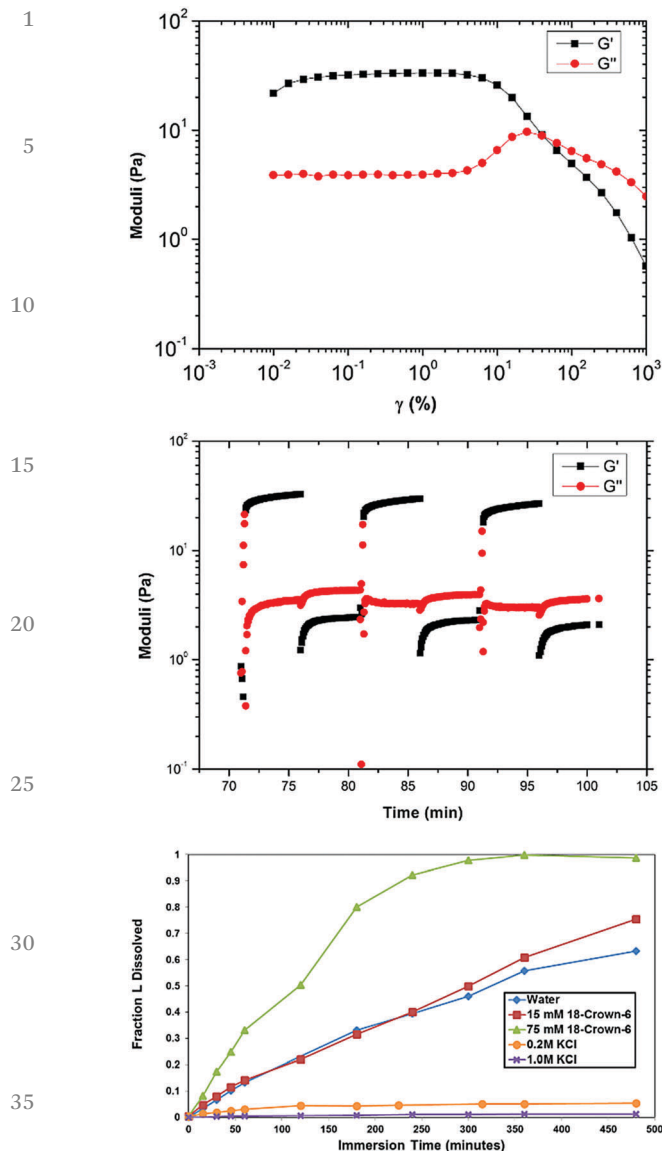

Fig. 1 Physical properties of gel **1** (10 mg mL^{-1} **HL**, 6 eq. K$_2$CO$_3$, 3.3 wt%), showing (a) manipulation of the gel with tweezers; (b) transparency of a gel monolith; (c) blue photoluminescence of the gel under ultraviolet irradiation (λ_{ex} = 366 nm), and (d) SEM image of the xerogel after coating on a silicon plate and drying under dynamic vacuum.

Fig. 2 (top) Strain sweep rheological experiment for gel **1** ($\omega = 1$ rad s^{-1}); (middle) recovery test for gel **1** at alternating strain amplitudes of 0.1 and 300%; (bottom) dissolution profiles for gel **1** measured by emergence of **L**$^-$ in the supernatant liquor by UV-Visible spectroscopy.

controlling gel breakdown in aqueous media through potassium sequestering agents, or the possibility of further stabilising the gel as a function of potassium ion concentration. Gel **1** was subjected to a series of experiments to quantitatively probe the gel dissolution process. By soaking a gel monolith in water or aqueous solutions of 18-crown-6 or KCl and measuring the emergence of dissolved **L**$^-$ in solution by UV-Visible spectroscopy, the gel dissolution kinetics were elucidated.

As shown in Fig. 2, a 1 mL monolith of **1** (10 mg mL^{-1}) added to 25 mL of water exhibits a half-life of *ca.* 5 hours. This is essentially unchanged for aqueous 18-crown-6 (15 mM), giving a slight acceleration compared to pure water only after 5–6 hours. Increasing the 18-crown-6 concentration to 75 mM resulted in a dramatic enhancement in dissolution rate ($T_{1/2} \sim 120$ min), and

a *ca.* 2.5-fold increase in initial rate. In contrast, immersing gel **1** in 0.2 M KCl solution led to only minimal dissolution, plateauing after *ca.* 2 hours with approximately 5% of the constituent **L** released from the gel. Similar results were observed in 1 M KCl solution; in both cases, the shape of the gel monolith was essentially unchanged after soaking for six weeks. This can most likely be ascribed to a combination of free potassium ions driving the phase equilibrium towards gelation, and the impact of ionic strength on the solubility of **L**$^-$ hindering the gel–sol reversion process.

We have shown that a heterotopic ligand **HL** forms a robust hydrogel **1** displaying a stimuli-responsive gel–sol reversion process. The unique combination of unsymmetric donor sites and strong aggregation tendency through π–π stacking interactions appears essential this function. The development of soft materials exhibiting rheological response to chemical stimuli is a key area of interest in materials science, which we are currently pursuing further.

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