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Fluorescent hydrogel formation from carboxyphenyl-terpyridine†

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We report the analysis of a novel terpyridine based supramolecular hydrogel which shows fluorescent properties in the gel but not in the sol form; the gel forms in a narrow pH range in aqueous solutions specifically in the presence of sodium ions, and contains between 98% and 99.2% water.

Terpyridines (terpys) are well known ligands for transition metal complexes, which find wide applications in supramolecular chemistry, dye sensitisation of photovoltaic cells, and in catalysis. The large diversity of physical properties such as luminescence and electrochemistry can be tuned by both changing the metal and the substitution pattern on the terpy ligand, making terpyridines very suitable building blocks in supramolecular chemistry.[1] In connection with other photoactive electron donor and acceptor moieties such as porphyrins,[2] terpy complexes have been shown to provide suitable systems for charge separation in artificial photosynthesis. In addition, a few specifically substituted terpyridine complexes have previously been shown to be good gelators in aqueous solutions, where metal complexation aids formation of the supramolecular gel network.[3] Hydrogels[4] have attracted general interest, for example due to their applications in medicine[5] for drug delivery,[6] as biological matrices for enzyme immobilisation[7] or in electrochemical capacitors.[8] However, the conditions for gel formation seem to depend strongly on several parameters such as substituents, concentration and salts used for all compounds investigated. We have found that 4′-*para*-phenylcarboxyl-2,2′:6′,2″-terpyridine **1** is able to form a reversible supramolecular hydrogel, which was observed during crystallisation attempts and is rather a serendipitous finding. The gel formed is opaque white and fluorescent under UV light, is thermally reversible and only formed in a narrow range of pH and terpyridine concentrations.

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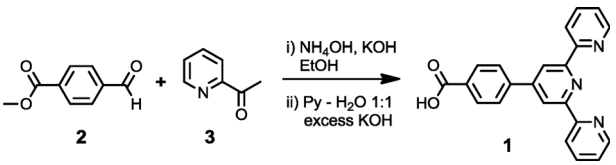
† Electronic supplementary information (ESI) available: Experimental details of synthesis, gelation, metallation and crystallisation of the terpyridine, SEM pictures and analytical data of the gels. CCDC 909638. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc37842f



Scheme 1 Synthesis of carboxy-terpyridine **1**.

The synthesis of **1** was performed according to literature procedures (Scheme 1)[9] from *p*-carboxy benzaldehyde **2** and 2-acetyl pyridine **3** in the presence of ammonia. After hydrolysis of the methyl ester using aqueous KOH and acidic workup, **1** readily forms a gel under specific conditions. Investigating the gelation further, a full set of conditions systematically varying the pH and the concentration of terpyridine **1** yielded a phase diagram which showed a very well defined set of conditions where the gel phase forms.† Both the concentration of sodium hydroxide and the concentration of the terpyridine are critical to gel formation. The gelation phase is defined between 0.5 and 0.75 M NaOH, and 8 to 20 mg mL^{-1} of the terpyridine in water, as shown in Fig. 1. Outside these boundaries, **1** either remains in solution or forms an insoluble precipitate with no visible higher order structure. This corresponds to a minimum water

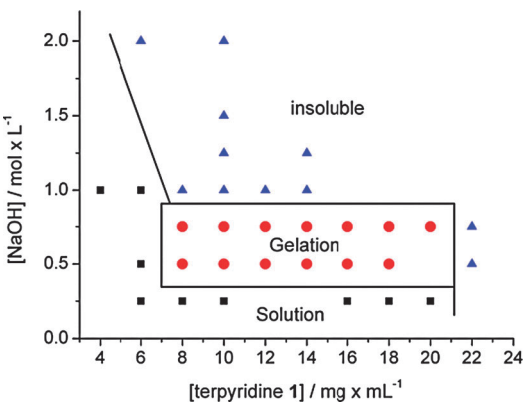


Fig. 1 Phase diagram of **1**, with conditions for forming clear solutions (■), gels (●) or insoluble aggregates (▲).

content of 98%, and an upper limit of 99.2% of water in the gel. It should be noted that gel formation was not observed when the protonated form of **1** was used, or if sodium was exchanged to ammonia or lithium; with potassium a gel was observed only upon storing at 4 °C overnight, thus gelation is very specific to Na^+. This might be explained by a preferential interaction of sodium with carboxylates compared to other cations (particularly lithium and potassium).[10] This is further corroborated by the observation that addition of an equal amount of 18-crown-6 per sodium induced complete dissolution of the gels within two days. Solvents other than water such as methanol, DMF or DMSO also did not induce gelation. The specific substitution pattern also seems to be crucial because replacing the carboxylate with bromide[11] inhibited gel formation, as did the attachment of sterically bulky groups such as *t*Bu at the terpyridine unit.

Spectral analysis showed that **1** has an absorbance at λ = 275 nm which does not significantly change on going from the sol to gel phase.† The luminescence spectra (λ_{ex} = 275 nm), however, revealed that in addition to an emission maximum at λ_{em} = 376 nm, a second peak at λ_{em} = 528 nm appears in the gel form, with a relative intensity of 18% compared to the first peak. We have used this characteristic gel emission peak to monitor the thermal behaviour as it provides us with an "all-or-nothing" handle; in particular reversibility and influence of the cooling rate on gelation (Fig. 2) were studied. At higher temperatures (>50 °C), the gel-phase melts and a clear solution of the terpyridine is present; the actual time to dissolve the gel is in the order of minutes, but is significantly longer at higher concentrations of **1**. Monitoring the emission at 528 nm at variable heating rates (0.5, 1 and 2 °C min^{-1}) showed consistent transitions at T_g = 42 °C (1 and 2 °C min^{-1}) or at 46 °C (0.5 °C min^{-1}). Gel formation, on the other hand, is strongly dependent on the cooling rate and a large hysteresis can be seen: gelation was observed at slower cooling rates, and at 2 °C min^{-1} no proper gel was obtained as seen by the weaker fluorescence of the system at 10 °C. Interestingly, heating of this intermediate state from 10 to 20 °C reinitiated the formation of a hydrogel. This behaviour is consistent for all systems investigated, thus is largely independent of the concentration of both NaOH and **1**. The hysteresis, and the gel formation dependence on the cooling rate but not on the heating rate, indicates that the supramolecular assembly is not at thermodynamic equilibrium during the annealing process.

One of the samples containing 10 mg mL^{-1} of **1** and 0.5 M NaOH was used to test additional water uptake.† The gel (0.5 mL) was layered with 250 μL of water and left to stand at room temperature. After considerable time (three weeks) the water phase still appeared to be separated from the hydrogel, thus the water was not taken up by the gel phase. However, upon tilting of the sample vial the water phase did not move.† Therefore a minimum amount of the terpy had diffused into the water phase turning it into a gel, which remained translucent and formed a clear separate gel phase compared to the opaque gel.

The structure of the gel was also examined using scanning electron microscopy (SEM).† The samples were dried under vacuum for the analyses. Depending on the initial gel forming conditions, a range of different morphologies were observed, but all mainly showing long non-crystalline fibrous structures with interconnecting thinner rod-like fibres. Fig. 3a and b show

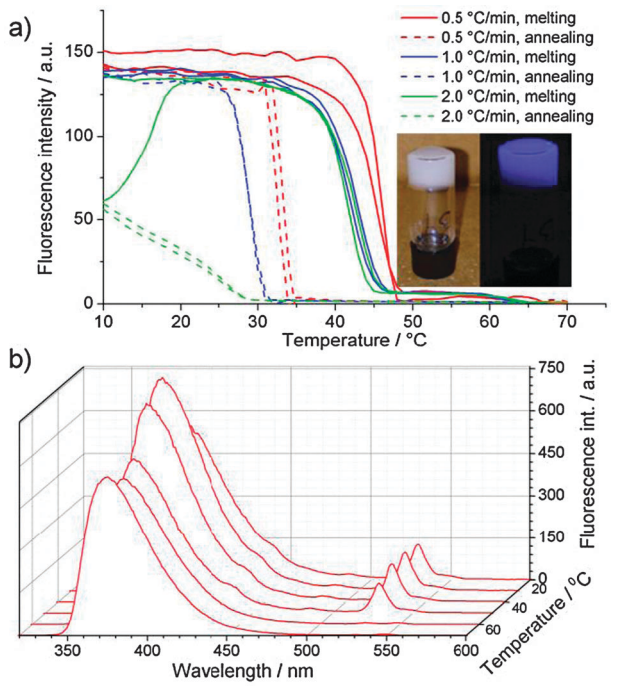


Fig. 2 (a) Melting (solid lines) and annealing (dashed lines) profiles at variable rates, measured by fluorescence emission (λ_{ex} = 275 nm; λ_{em} = 528 nm). The inset shows the fluorescent gel under a hand-held UV lamp. (b) Change in the fluorescence spectrum upon cooling (front to back).

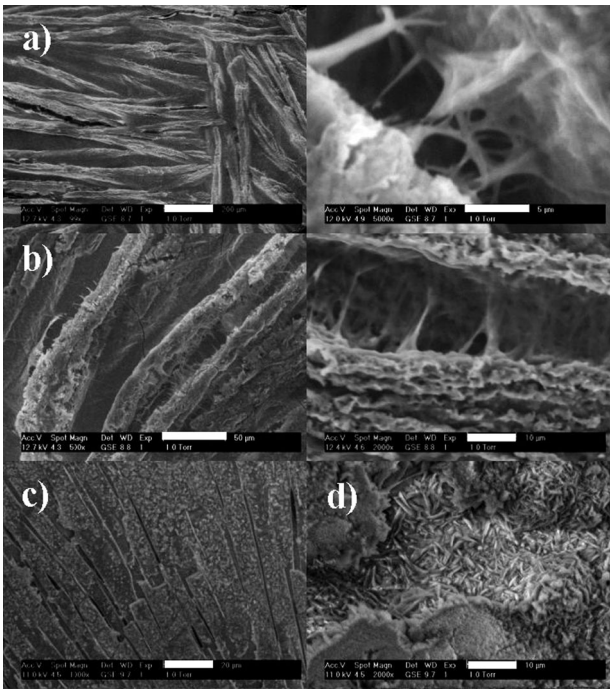


Fig. 3 Representative SEM images of the fresh gels: (a) [**1**] = 9 mg mL^{-1}, [NaOH] = 0.5 M, scale bar left: 200 μm, right: 5 μm. (b) [**1**] = 5 mg mL^{-1}, [NaOH] = 0.5 M, scale bar left: 50 μm, right: 10 μm. SEM images of aged samples: (c) [**1**] = 4 mg mL^{-1}, [NaOH] = 0.75 M, scale bar: 20 μm. (d) [**1**] = 8 mg mL^{-1}, [NaOH] = 0.75 M, scale bar: 10 μm.

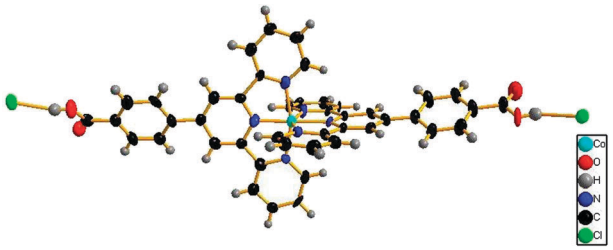


Fig. 4 XRD structure of $Co(\mathbf{1})_2(Cl)_2$ (atoms are drawn at the 50% probability level after anisotropic refinement).

some representative examples of the SEM pictures obtained. These seem to be the preferred morphologies for the freshly formed terpy gels. Upon ageing for several weeks in air, the morphology of the gels alters significantly, and either columnar structures or formation of micro-crystalline structures were observed (Fig. 3c and d). The gels obviously rearrange their structure over time when exposed to moist air.

Since the terpyridine is a versatile ligand for transition metals, and some further substituted complexes have shown gelation,[3b,12] we also investigated whether metal complexation has an influence on the behaviour of **1** towards hydrogel formation. We studied both cobalt and copper due to their ease of formation, and the complexes were made *in situ*. A 0.5 : 1, 1 : 1 and 2 : 1 mixture of metal chloride to **1** was used for the formation of the complexes, using either water or DMF as solvent. The formation of the complexes could be detected using UV-vis spectroscopy, but they remained largely insoluble in water or DMF, thus gelation was not occurring with these systems. Similarly, preformed ruthenium or platinum complexes were not soluble enough under the gelation conditions. However, we were able to grow single crystals of the $Co(\mathbf{1})_2^{2+}$ complex from the DMF solution, a complex which was previously not analysed by single crystal XRD (Fig. 4).‡ The complex forms a distorted octahedral meridional complex and crystallises as the di-chloride with six solvent DMF molecules. Both chlorides are hydrogen bonded to the adjacent carboxylate hydrogens and a 3D network is supported by C–H···Cl contacts. The DMF molecules sit in pockets within the structure. The crystals lost solvent very rapidly, therefore the rather low quality of the diffraction and the structure refinement did not allow for further detailed analysis of the structure. However, the fact that the metallated terpyridines crystallise rather than forming a gel supports the fact that a planar structure is essential for gelation and π-stacking plays a central role in the process.

In summary, the metal ligand 4′-*para*-phenylcarboxy-terpyridine **1** has been shown to form a thermally reversible fluorescent gel with a water content of up to 99.2%. The gelation is likely due to efficient π–π stacking of the hydrophobic terpy units, combined with formation of the sodium induced salt bridge between terpy-carboxylates and hydrogen bonded networks with the enclosed water clusters and between the terpy units, as was observed previously with pyridine systems.[13] In their case, intermolecular hydrogen bonding with weak π–π stacking was accounted for fluorescence in the gel, which could equally be the case in our system. The gel forms in a narrow range of pH and terpy concentration, and the melting transition can be varied to a limited extent. The gel does not swell upon addition of further water but rather some of the terpy diffuses into a supernatant water layer, transforming the water layer into a gel of different consistency instead. Metal binding to give both M(**1**) and M(**1**)$_2$ complexes (M = Co^{III}, Cu^{II}) inhibits gel formation, most likely due to the coordination geometry on the metal which acts as a sterical barrier; bulky groups at the periphery of the terpy also inhibit gel formation as does removal of the carboxy group. The XRD structure of the cobalt complex could be solved, which demonstrates that the octahedral environment around the cobalt centre is not suitable for efficient π–π stacking of the terpy units. The gels are now under investigation for further applications in electrochemistry and ion transport, because the terpy unit could be used as an electrochemically active sensor moiety in gel-loaded electrodes.

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Notes and references

‡ Data were collected on a Bruker Nonius KappaCCD using a Mo rotating anode generator; standard procedures were followed. The crystals lost solvent very rapidly and data collection, structure solution and refinement were very problematical, however the basic structure is clear. Crystal data for 2011sot0106 (AG/6043/33/F2) $C_{62}H_{72}Cl_2CoN_{12}O_{10}$, M_r = 1275.15, T = 120(2) K, triclinic, space group $P\bar{1}$, a = 8.7683(15), b = 18.903(3), c = 19.765(4) Å, α = 76.568(10), β = 80.430(10), γ = 85.719(11)°, V = 3139.8(10) Å^3, ρ_{calc} = 1.349 g cm^{-3}, μ = 0.426 mm^{-1}, Z = 2, reflections collected: 16592, independent reflections: 8528 (R_{int} = 0.0778), GOF = 1.961, final R indices [$I > 2\sigma(I)$]: R_1 = 0.1998, wR_2 = 0.4262, R indices (all data): R_1 = 0.2688, wR_2 = 0.4543, largest difference peak and hole = 0.975 and −0.865 e Å^{-3}.

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