Fluoride-responsive organogelator based on oxalamide-derived anthraquinone†

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Anthraquinone derived oxalamide gelator 1 forms with aromatic solvents and alcohols very stable gels which selectively respond to the presence of fluoride anion by colour change and/or gel-to-sol transition.

Low molecular weight organic compounds capable of forming gels with water and various organic solvents have recently received considerable attention.[1] Solvent gelation is generally a consequence of the formation of 3-dimensional gel networks constituted by the entanglement of many fibers. It is well documented that gel fibers are formed by the predominantely unidirectional self-assembly of gelator molecules through intermolecular hydrogen bonding, aromatic stacking, lipophilic and electrostatic interactions. Gels are dynamic soft materials in a state that lingers between solution and the solid state. For that reason gels are considered very promising for new applications in materials science. In particular, many efforts are devoted to the development of stimuli responsive gels, whose properties can be either switched on–off or tuned by an external or internal chemical or physical stimulus.[2] Such responsive systems are highly desirable for the development of sensor devices or in applications like drug delivery or catalysis.

Fluoride anion is one of the most significant targets for sensing because of its importance in many biological and industrial systems.[3] Therefore, a large number of sensors for fluoride anion have been reported to date which, however, operate in solution.[4]

We have recently described oxalamide-based gelators capable of forming various organo- as well as hydrogels.[5] This type of gelator self-assembles into fibrous aggregates through the cooperative and unidirectional hydrogen-bonding of oxalamide units. Here we report on the preparation of the anthraquinone based oxalamide gelator **1** (Fig. 1), which possesses pronounced gelling properties and exhibits selective binding of fluoride ion. This selectivity makes it the first example of a fluoride responsive gel system which allows naked-eye detection of fluoride by colour change or gel-to-sol transition. In addition the properties of its regioisomer **2**, and the model compounds **3** and **4** have been investigated. Systems containing an anthraquinone group have previously been reported as colorimetric sensors for anions.[6]

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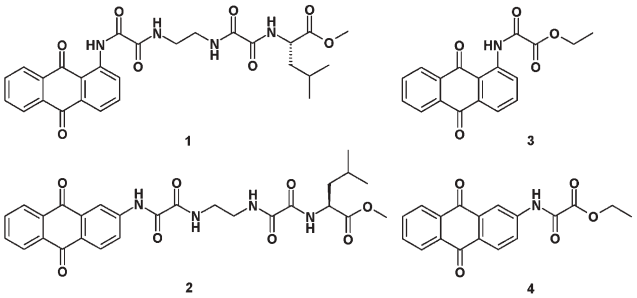

Fig. 1 Structures of the anthraquinone derivatives **1–4**.

The gelation properties of **1** and **2** were assessed using various organic solvents. They are scarcely soluble and a co-solvent was required. Typically, the compounds were first dissolved in the minimal volume of DMF after gentle heating and then the selected solvent was added. After cooling to ambient temperature, the vessel was turned upside down. When the fluidity of the system was absent, it was denoted as a gel (Table 1).

The results in Table 1 show that the anthraquinone derivative **1** possesses excellent gelation properties toward aromatic solvents and alcohols, which could be gelled at concentrations as low as 1.0 mM. All prepared gels are greenish yellow and transparent. Surprisingly, we have found that regioisomer **2** was incapable of forming gels with any of the tested solvents. This observation shows that the position of substitution at the anthraquinone ring has a pronounced influence.

The morphology of the *p*-xylene gel was investigated by transmission electron microscopy (TEM). The presence of a gel network structure consisting of many entangled tape-like aggregates of widths between 20–90 nm and lengths of several μm is shown in Fig. 2a. Atomic force microscopy (AFM) images of diluted *p*-xylene and EtOH gels are in agreement with the tape-like morphology of the aggregates, as observed in the TEM images.

Table 1 Results of gelation tests for **1** and **2**[a]

Solvent	1	2
DMSO	S	S
DMF	S	P
Ethanol	G (1.0)	P
1-Butanol	G (1.2)	P
Acetonitrile	G (2.6)	I
Benzene	G (14.4)	P
Toluene	G (4.2)	P
p-Xylene	G (1.3)	P
Decalin	G (1.4)	P
Cyclohexane	S	P

[a] S, solution; P, precipitate; G, transparent gel; I, insoluble. Numbers in parentheses present the minimal gelation concentration (mgc) in mM.

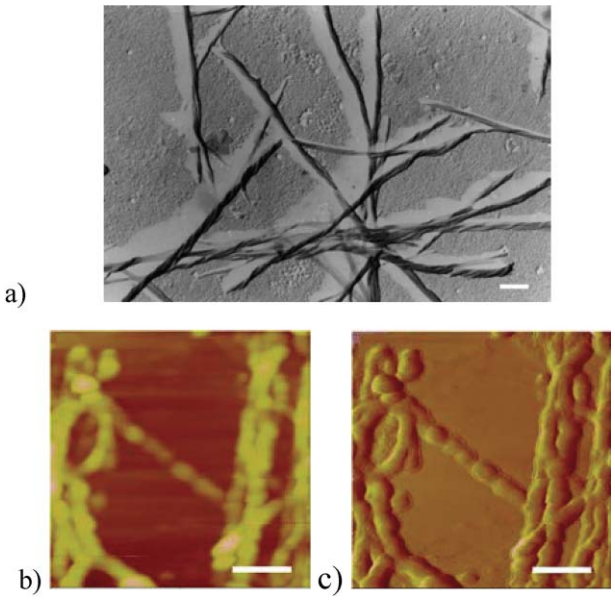

Fig. 2 a) TEM image of Pd shadowed **1**–*p*-xylene gel and AFM topography (b) and signal error images (c) of diluted **1**–EtOH gel (scale bars = 100 nm).

The detailed cross-sectional analysis shows the presence of isolated and randomly twisted tapes of 18–50 nm and 10–38 nm in diameter for *p*-xylene and EtOH diluted gels, respectively (Fig. 2b,c).

Since **1** is an efficient gelator of both protic and aromatic solvents, we believe that both anthraquinone stacking and oxalamide hydrogen-bonding interactions contribute to the stabilization of the self-assembled aggregates. To obtain further insight we measured FTIR and UV-Vis spectra of the **1**–*p*-xylene gel at different temperatures. The FTIR spectra at room temperature showed the presence of bands belonging to hydrogen-bonded (3290 cm^{-1}) and free (3351 cm^{-1}) NH groups, respectively. At high temperatures, the intensities of the hydrogen bonded NH bands decreased while those of the free NHs increased. These observations clearly show that at least some of the NHs of the two oxalamide groups are involved in intermolecular hydrogen bonding. Absorption spectral changes of gelator **1** in *p*-xylene and EtOH gels at variable temperature were also monitored (Fig. S1a,b in the ESI†). The thermoreversibility of the gelation process was confirmed by several repeated variable-temperature measurements with the same sample. Comparison of the spectra at 25 and 95 °C of the EtOH gel, revealed that the absorption band at 421 nm at 25 °C was hypsochromically shifted to 391 nm at 95 °C and its intensity was increased. Similar behaviour was found in the case of *p*-xylene gel, where the 414 nm band at 25 °C was shifted to 387 nm at 85 °C with the completion of the gel to sol transition. Such temperature-dependent spectral changes indicate the presence of π–π stacking interactions between anthraquinone units in the gel which unstack upon heating.

The anion-binding properties of **1** and **2** toward a number of selected target anions (namely, F^-, Cl^-, Br^-, I^-, CH_3COO^-, $H_2PO_4^-$) were examined in DMSO. Compounds **1** and **2** showed intense variation of their electronic absorption spectra upon addition of tetrabutylammonium fluoride (TBAF) at 25 °C (Fig. 3 for **1** and Fig. S3 in the ESI† for **2**). The new absorption bands (abs. maxima at 481 nm and 493 nm for **1** and **2**, respectively)

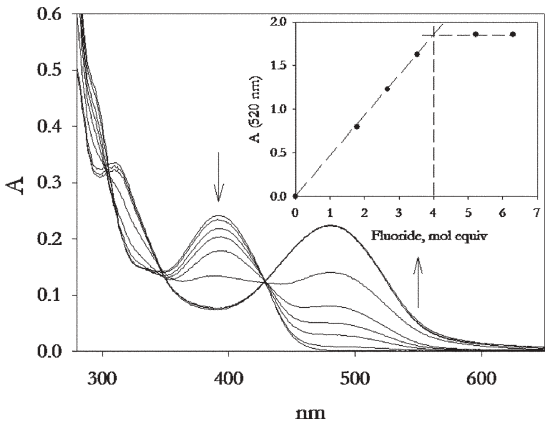

Fig. 3 UV-Vis spectral changes observed for **1** (4.4×10^{-5} M) upon addition of fluoride anion in DMSO at 25 °C. Inset shows the absorbance at 520 nm as a function of F^- concentration added (**1** = 4.75×10^{-4} M).

which arose upon the addition of F^- are responsible for vivid colour changes visible to the naked-eye at concentrations as low as 0.1 mM (see the ESI†). Both **1** and **2**, showed good affinity for fluoride, as demonstrated by the linear dependence of their absorbance *vs.* fluoride concentration which reaches a plateaux after 4 equivalents of F^- have been added.[7] Amidic NHs are good hydrogen-bond donors and are widely exploited as binding sites for anion recognition.[8] Therefore, it is not surprising that **1** and **2**, which possess four amidic NH have a strong affinity for fluoride anion. It should be noted that only the NH directly linked to the anthraquinone moiety is responsible for the colour change, at variance with the other NHs which are active in binding but their interaction with F^- does not directly induce any variation in the visible part of the spectrum. As pointed out by Fabbrizzi *et al.*, fluoride can act as a strong base in DMSO[9] and deprotonation of at least the most acidic NH (close to the anthraquinone ring) can likely be the final consequence of the fluoride binding to **1** and **2** (Fig. S4, ESI†). Among the halide series, no other anion showed affinity for **1** and **2** in DMSO solution. The selectivity of **1** for fluoride is even more pronounced since it does not show any significant variation of its absorption spectrum in the presence of several equivalents of either phosphate ($H_2PO_4^-$) or acetate. At variance with **1**, the isomeric **2** showed spectral changes upon addition of either phosphate and acetate, but less intense than those observed with fluoride (Fig. S5, S6 in the ESI†). Molecular modelling showed that the minimized conformation of **1** contains a strong intramolecular hydrogen-bond formed between the anthraquinone bound N–H and the vicinal anthraquinone carbonyl oxygen leading to planarization with the first oxalamide unit. Such a hydrogen bond is not possible for **2** and this makes the NH more available for hydrogen bonding with phosphate or acetate oxygens (Fig. S7, ESI†). In the ^{1}H-NMR spectra of **1** and **2** the anthraquinone-NH protons appear at δ 13.45 and 11.30 ppm, respectively. Hence, a strong downfield shift of **1**-NH is consistent with the presence of a stable intramolecular hydrogen bond.

A quantitative analysis of the binding and a precise measurement of the association constants is complicated by the existing multiple equilibria since each of the four NHs competes for the anion. An estimation of the binding affinities of the most acidic NHs in **1** and **2** can be provided taking into account the binding data with the model compounds **3** and **4** (see the ESI†).

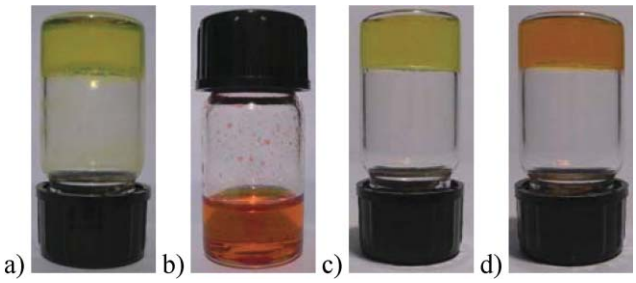

Fig. 4 (a) **1**–*p*-xylene gel; (b) addition of 10 equivalents of TBAF to the hot *p*-xylene solution of **1** followed by cooling to rt; (c) **1**–EtOH gel; (d) reddish **1**–EtOH gel after addition of 10 eqivalents of F^-.

The effect of anion binding on the gelation process was monitored by repeating the gelation experiment of **1** in *p*-xylene and EtOH in the presence of 10 equiv. of fluoride anion (Fig. 4). Gelator **1** (2.8×10^{-3} M) and 10 equiv. of TBAF were added to a screw-capped vial containing *p*-xylene or EtOH (2 mL) and the mixture was gently heated until a clear solution was obtained.

After cooling, a reddish *p*-xylene solution was obtained instead of a gel (Fig. 4b). In this system fluoride is poorly solvated by the lipophilic *p*-xylene and it can compete well for the gelator NH groups. This leads to the disruption of the intermolecular hydrogen bonds which stabilize the gel architecture and results in a total inhibition of gel formation. Instead, the hot ethanol solution upon cooling turned back into a reddish coloured gel in spite of the presence of F^- (Fig. 4d). The better solvation of fluoride in a polar protic solvent makes it a less efficient competitor for the gelator NH groups. Accordingly, the intermolecular hydrogen bonding is only partly influenced and the gel is still preserved.

The addition of chloride, phosphate or acetate to hot *p*-xylene and EtOH solutions of **1** does not disturb the formation of gels and does not produce any colour change, in accordance with a negligible affinity of **1** for such anions.

The presence of fluoride not only prevents the formation of gel in *p*-xylene, but can actively disrupt a preformed gel, as shown by the experiment in Fig. 5. The deposition of a concentrated solution of TBAF in *p*-xylene (50 equiv.) on top of the **1**–*p*-xylene gel immediately produces a gel-to-sol transition in the interphase region. This process progresses in time by diffusion until the final gel is totally disrupted after 4 h.

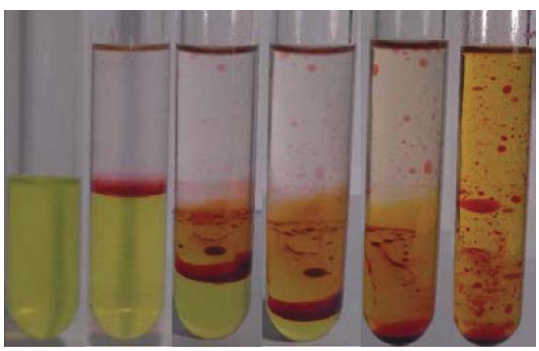

Fig. 5 Diffusion of fluoride from a concentrated *p*-xylene solution (50 equiv.) through the **1**–*p*-xylene gel. From left to right: **1**–*p*-xylene gel; immediately after addition of TBAF solution; after 2, 3 and 4 h; and overnight standing.

In conclusion, we have synthesized and studied the properties of the new anthraquinone derived oxalamide gelator **1**. It showed an excellent gelation ability towards aromatic solvents and alcohols at very low concentrations. We also demonstrated that the gel phase is responsive to the presence of fluoride which leads to a colour change in the **1**–EtOH gel and totally prevents gelation of the **1**–*p*-xylene system. Interestingly, fluoride is able to induce the gel-to-sol transition simply by contact with gel in *p*-xylene.

We believe that the fluoride responsive gels reported here may provide the basis for the development of non-fluid and more robust gel-based systems for sensing fluoride with the naked eye. Further studies along this direction are in progress, especially to fully exploit the photo- and electrochemical properties of the anthraquinone moiety embedded in a gel matrix which may endow new properties in multiresponsive gel systems.

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