ChemComm

COMMUNICATION

Cite this: *Chem. Commun.*, 2014, **50**, 3064

Received 9th December 2013,
Accepted 7th January 2014

DOI: 10.1039/c3cc49323g

www.rsc.org/chemcomm

Transition from low molecular weight non-gelating oligo(amide-triazole)s to a restorable, halide-responsive poly(amide-triazole) supramolecular gel†

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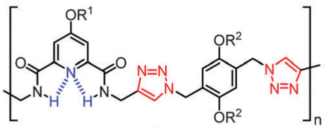
A self-assembled poly(amide-triazole) physical gel (1) was found to show responsive behaviour towards halide anions, while the corresponding monomeric (2) and dimeric homologues (3) were non-gelating. In the presence of halide anions, polymer gel 1 collapsed to become a solution, but could be restored back to the gel state after addition of a $AgNO_3$ salt.

Supramolecular self-assembled gels that show responsive behaviour towards external stimuli are highly interesting compounds because they can function as molecular sensors, diagnostic agents and materials for drug delivery and tissue engineering.[1] These gelating materials are generally prepared from low molecular weight (LMW) compounds which form thermo-reversible physical gels due to non-covalent self-assembly.[2] On the other hand, polymer chemical gels, in which the gel network is constructed *via* covalent crosslinking, generally lack responsive properties towards external stimuli as the network structure is very stable as the gelation process is irreversible.[3] Hence, polymer gels that exhibit responsive properties are rare. In the literature, there are only a few examples of stimuli-responsive polymer physical gels, in which the gelation is based on non-covalent interactions.[4] We earlier reported the synthesis and thermo-reversible organogelating property of polymer **1**.[5] In our previous study attention was focused mainly on the conformational rigidity of the intramolecularly H bonded pyridine-2,6-dicarboxamide unit on the polymerization efficiency of click polymerization. It was found that the presence of such rigid units in the polymer backbone not only produced polymers with higher polymerization efficiency, but also conferred them with gelation properties. Hence, structurally similar polymers lacking this kind of conformational rigidity due to the removal of the pyridine nitrogen or amide NH did not possess gelating properties. Since triazole-rich compounds are known to interact with anions *via* H bonding,[6] therefore we were interested to investigate the anion binding properties of polymer **1**. Herein we report a rare example that polymer **1** based on the amide-triazole repeating unit was found to be a halide-responsive physical gel, whereas its monomeric **2** and dimeric **3** homologues possessing the same repeating unit were found to be devoid of gelation properties.[7] Furthermore, physical gel **1** was found to collapse and become a solution after treatment with halide anions, but could be restored to its gel form upon addition of silver ions.



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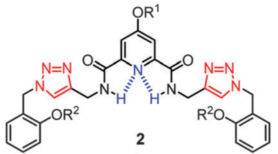

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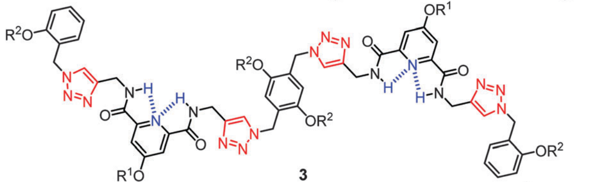

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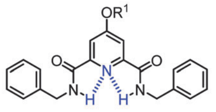

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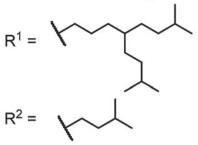

In order to have a better understanding of the anion binding capability of polymer **1**, its LMW homologues **2–4** were prepared. Compounds **2** and **3** actually represent the corresponding monomer and dimer of polymer **1**, while **4** is the monomeric analogue without the triazole units in the binding motif. The synthesis and structural characterization of LMW homologues **2–4** are described in the ESI.† In contrast to literature precedents,[8] none of these LMW compounds were organogelators, but they were all shown to interact with halide anions. The host–guest chemistry of **2** and Cl^- was investigated by ^1H NMR titration experiments involving the addition of tetrabutylammonium chloride (TBACl) to a $[D_8]$-THF solution of **2** (2.6 mM), and significant downfield shifts of the amide

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† Electronic supplementary information (ESI) available: Synthesis and characterization data for all new compounds; determination of binding constants. See DOI: 10.1039/c3cc49323g

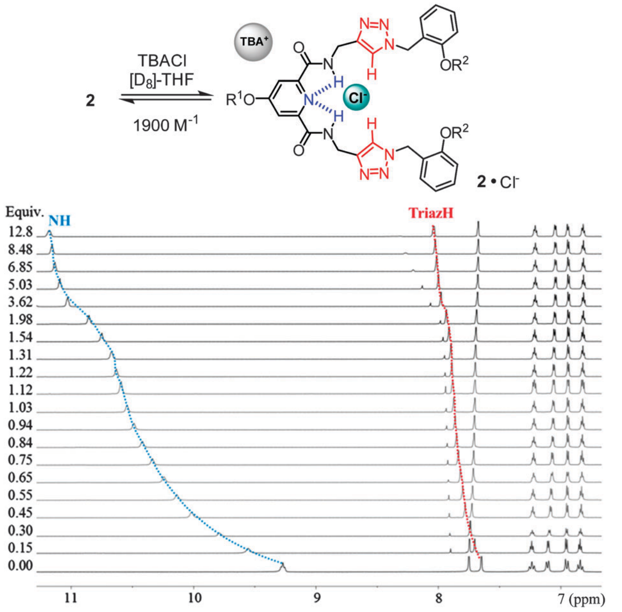

Fig. 1 Stacked partial ^{1}H NMR spectra ([D$_8$]-THF, 700 MHz) of compound **2** upon addition of TBACl.

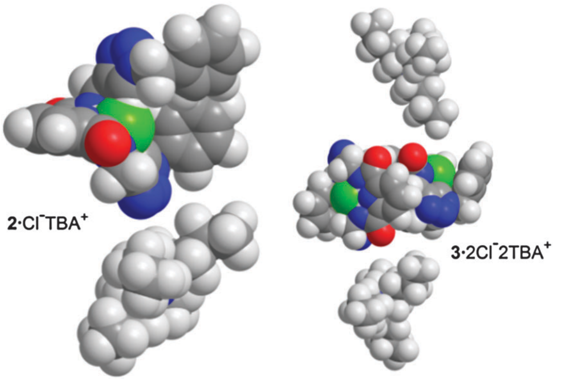

Fig. 2 Space filling models of **2**·Cl$^-$ TBA$^+$ (left) and **3**·2Cl$^-$ 2TBA$^+$ (right) (grey: C; white: H, red: O; blue: N; green: Cl). The alkoxy side chains were omitted for clarity.

NH (Δδ ~1.5 ppm) and triazole CH (Δδ ~ 0.4 ppm) signals were observed (Fig. 1), indicating that both of them were interacting with the Cl$^-$. The corresponding Job plot confirmed that the binding stoichiometry was 1 : 1.[9] Hence, it was proposed that **2** folded into a hairpin-like structure to create a "binding site" for Cl$^-$ (Fig. 2). The chemical shift values of the amide NH signal were then fitted to a 1 : 1 binding model,[10] and the binding constant (K_a) of **2** for Cl$^-$ was found to be 1930 ± 150 M^{-1}.[9] Similarly, the K_a values of **2** for Br$^-$ and I$^-$ were determined to be 310 ± 10 M^{-1} and 31 ± 2 M^{-1}, respectively, upon titration with TBABr and TBAI.[9] These values were comparable to those of other open-chain analogues reported before.[11] The gradual decrease of the binding constants towards the larger halide anions suggested that the binding pocket had a relatively small cavity, and was best fitted to the smallest Cl$^-$. Incidentally, compound **4** without the two triazole units also binds to Cl$^-$, albeit with a lower binding constant (1530 ± 50 M^{-1}).[9] This implied that the presence of the triazole CHs enhanced the binding of halide anions. As compound **2** showed the strongest association towards Cl$^-$, our subsequent investigations were then focused only on this anion.

Our next attention was then turned to the dimeric receptor **3** with two binding sites, which could be considered as the simplest prototype that possessed multiple binding sites. In particular, it was interesting to know if the two binding sites could bind two halide anions independently or whether allosteric binding can occur. As expected, the amide NH and triazole CH resonance signals showed a similar downfield shift upon addition of TBACl.[9] A Job plot analysis showed that **3** bound to Cl$^-$ in a 1 : 2 stoichiometry.[9] The chemical shift values of amide NH were then fitted to a 1 : 2 binding model,[9,10] and the K_1 and K_2 were found to be 100 ± 10 and 740 ± 120 M^{-1}, respectively. The K_1 value should not be directly compared to the K_a value of the monomer **2**–halide complex, as K_1 is affected by the second binding process. In principle, the interaction parameter α, defined as $4K_2/K_1$, should be <1, $=1$, >1, for positive allosteric, non-cooperative, and negative allosteric bindings, respectively.[10] In our case, the α value was 30, indicating that binding of the first Cl$^-$ enhanced the binding of the second.[12] A Hill plot was constructed and the Hill coefficient was 2.0,[9] reinforcing the fact that positive allosteric binding was indeed happening. At this moment, we were uncertain of the mechanism of such positive allosteric interaction since the two binding sites appeared to be isolated from each other. One possible explanation could be an induced structural reorganization of the second binding site after the first Cl$^-$ binding, providing better shape complementarity to the second Cl$^-$ binding.

Due to the inherent structural heterogeneity of polymer **1**, it was difficult to obtain its binding constant towards halide anions. Nonetheless, based on the study on the dimeric species **3**, it was believed that positive allosteric binding should also exist in the polymer system. Similar to the findings for oligomers **2** and **3**, ^{1}H NMR titration experiments revealed significant downfield shifts of the amide NH and triazole CH signals upon addition of TBACl to a [D$_8$]-THF solution of **1** (Fig. 3). Furthermore, it was found that the polymer–chloride complex gave sharper ^{1}H resonance signals than that of pure polymer **1** itself, suggesting the breakdown of interpolymer chain H bonding interaction upon Cl$^-$ binding.

Interestingly, treatment of a 2% w/v polymer toluene gel **1** with TBA salts of halide (Cl, Br and I) triggered a gel-to-sol transition. It was found that 0.2 equiv. (with respect to the total number of binding sites) of TBACl, 0.3 equiv. of TBABr, or 0.5 equiv. of TBAI, were

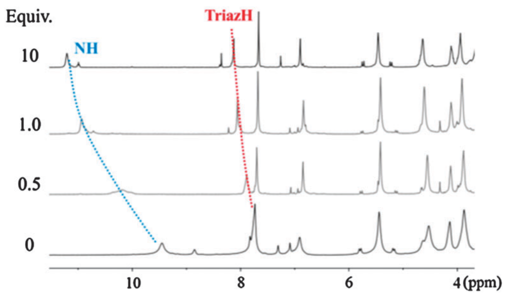

Fig. 3 Stacked partial ^{1}H NMR ([D$_8$]-THF, 400 MHz) spectra of **1** upon addition of TBACl.

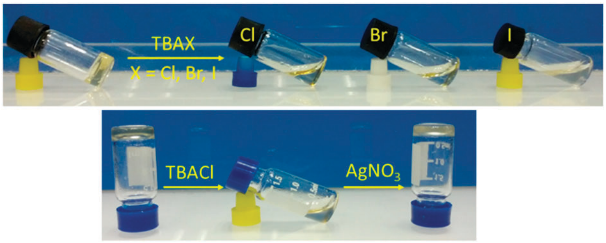

Fig. 4 (top) Gel-to-sol responsive behaviour of polymer toluene gel **1** upon addition of TAB salts of halide. (bottom) Sol-to-gel responsive behaviour of polymer **1**–Cl$^-$ complex upon addition of a AgNO$_3$ salt.

required for the complete breakdown of the gel (Fig. 4, top), in which the whole process was completed within hours.

FTIR studies were then performed to reveal the H bonding environment of the oligomer–halide and the polymer–halide complexes.[9] Upon addition of one equiv. of TBACl to a THF solution of monomer **2**, the NH stretching frequency was significantly red shifted (from 3315 to 3170 cm^{-1}). A similar red shift of the NH stretching frequency (from 3313 to 3182 cm^{-1}) was also noted when TBACl was added to polymer **1** in THF. These observations indicated the weakening of the NH stretching due to the formation of the H bond between the amide NH and Cl$^-$. Moreover, there was almost no change in the C=O stretching frequencies upon addition of TBACl, which provided evidence that Cl$^-$ binding was *via* the NH but not the C=O functionality. Unfortunately, we were unable to monitor the triazole CH stretching due to background absorption of the THF solvent (2700–3150 cm^{-1}).

The halide-responsive property of polymer gel **1** could be rationalized by replacement of the inter-polymer chain H bonding network with the NH···halide and triazole–CH···halide H bonding complex, which resulted in the segregation of individual polymer chains. Incidentally, SEM images of the air-dried **1**–chloride complex showed segregated polymer fibers clearly, which provided additional evidence of the proposed breakdown of the gelating network upon Cl$^-$ complexation (Fig. 5).

The gelation power of the polymer–halide complex could be restored by competitive removal of the Cl$^-$. Hence, upon addition of a slight excess (1.5 equiv. with respect to Cl$^-$) of AgNO$_3$ powder to a 2% w/v polymer–halide complex solution in toluene, a translucent gel was formed after a warming and cooling process (Fig. 4, bottom). It was suggested that the Ag$^+$ ion removed the Cl$^-$ from the polymer–Cl$^-$ complex, thus the polymer regained its abilities to re-form the gelation network *via* interpolymer chain H bonding. Unfortunately, it was found that such reversible halide-responsive gelation behavior could not be repeated for the second time as the insoluble AgCl and TBAX salts perturbed subsequent gel formation.

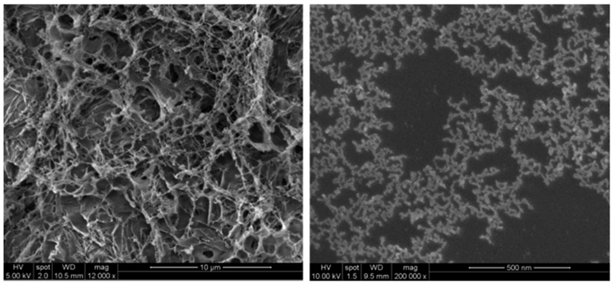

Fig. 5 SEM image of a freeze-dried sample of **1** at 12 K magnification (left) and an air-dried polymer **1**–Cl$^-$ complex from toluene at 200 K magnification (right).

In summary, we reported a rare example of a restorable, halide anion-responsive polymer physical gel **1** based on reversible H bonding interactions. This work also highlights a few advantages of using polymer-based materials for chemo-sensing applications. First, polymers may exhibit properties (*e.g.* gelation as in this case) whereas their LMW oligomeric homologues do not. Second, the presence of multiple binding sites in a polymer can promote positive allosteric binding affinity towards guest molecules and can improve its sensitivity. Both of these are useful attributes associated with polymer-based sensors and carrier systems.

The work was supported by grants from the RGC (CUHK 400810) and partially from the UGC (AoE/P-03/08) of HKSAR.

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