



HAL
open science

A water-soluble supramolecular polymeric dual sensor for temperature and pH with an associated direct visible readout

Aurélie Malfait, Fanny Coumes, David Fournier, Graeme Cooke, Patrice Woisel

► To cite this version:

Aurélie Malfait, Fanny Coumes, David Fournier, Graeme Cooke, Patrice Woisel. A water-soluble supramolecular polymeric dual sensor for temperature and pH with an associated direct visible readout. *European Polymer Journal*, 2015, 69 (23), pp.552-558. 10.1016/j.eurpolymj.2015.02.033. hal-02484467

HAL Id: hal-02484467

<https://hal.science/hal-02484467v1>

Submitted on 8 Dec 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



A water-soluble supramolecular polymeric dual sensor for temperature and pH with an associated direct visible readout

Aurélie Malfait^a, Fanny Coumes^a, David Fournier^a, Graeme Cooke^{b,*}, Patrice Woisel^{a,*}

^a Université Lille Nord de France, Unité des Matériaux Et Transformations (UMET, UMR CNRS 8207), Ingénierie des Systèmes Polymères (ISP), 59655 Villeneuve d'Ascq Cedex, France

^b Glasgow Centre for Physical Organic Chemistry, WestCHEM, School of Chemistry, Joseph Black Building, University of Glasgow, Glasgow, G12 8QQ, UK

ARTICLE INFO

Article history:

Received 15 January 2015

Received in revised form 18 February 2015

Accepted 19 February 2015

Available online 26 February 2015

Keywords:

RAFT process

Host-guest interaction

Supramolecular chemistry

Dual sensor

Multi stimuli responsive polymer

Visible readout

ABSTRACT

We report a multi-stimuli responsive polymeric sensor consisting of a pseudorotaxane-like architecture fabricated from a 1,5-diaminonaphthalene end-functionalized poly(*N*-isopropyl)acrylamide (**Napht-N-PNIPAM**) and cyclobis(paraquat-*p*-phenylene) (**CBPQT⁴⁺**, **4Cl⁻**). The coloured nature of the poly-pseudorotaxane provides a sensor for temperature and pH in water with an associated visible readout. To create this dual responsive polymeric sensor, a new chain transfer agent (**Napht-N-CTA**) incorporating a pH-responsive 1,5-diaminonaphthalene unit was synthesized and used for the polymerization of *N*-isopropylacrylamide via Reversible Addition-Fragmentation Chain Transfer (RAFT). The ability of **Napht-N-PNIPAM** to form a pseudorotaxane architecture with **CBPQT⁴⁺**, **4Cl⁻** in aqueous media was studied by means of UV-Vis, NMR (¹H, 2D-ROESY, DOSY) and ITC experiments. Interestingly, the pseudorotaxane architecture can be reversibly dissociated upon either heating the sample above its cloud point or protonating the nitrogen atoms of the 1,5-diaminonaphthalene-based guest unit by adjusting the pH to around 1. In both cases a dramatic colour change occurs from intense blue-green to colourless.

© 2015 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Stimuli-responsive polymeric materials have attracted considerable attention and have become a much studied sub-discipline in contemporary polymer chemistry [1–6]. This burgeoning field has significantly benefitted by advances in controlled (radical) polymerizations, which has led to rapid development of novel stimuli-responsive polymers with bespoke and well-defined (macro)molecular architectures with largely predictable physico-chemical properties. The growing interest in smart polymers able to respond to different stimuli including: temperature, light, pH, ionic strength, and analyte

concentration has led to the development of functional polymers with a range of new applications [7–14], including smart drug delivery systems for instance [15–17]. In addition, the last decade has provided stimuli-responsive polymers capable of sensing and responding to environmental changes or the presence of analytes. Compared to their molecular-scale brethren, macromolecular based sensors offer several advantages including improved detection sensitivity, better dispersibility in aqueous media, and flexibility of processing thus facilitating their integration into viable devices.

Temperature and pH play a central role in many fields of science and engineering, and as a consequence, attention has been directed towards the design of smart polymeric systems capable of monitoring these two parameters. Usually these polymeric sensor systems incorporate reporter units which take advantage of the intrinsic

* Corresponding authors.

E-mail addresses: graemec@chem.gla.ac.uk (G. Cooke), patrice.woisel@ensc-lille.fr (P. Woisel).

responsiveness of polymers to their microenvironment such as the structural changes that accompany temperature (e.g. Lower Critical Solution Temperature, LCST) or pH changes. Although numerous responsive polymer matrices incorporating either temperature or pH sensitive fluorescent probes have been reported in literature [18–24], it is noteworthy that very few dual-fluorescent sensors capable of monitoring both temperature and pH changes have been described in literature [25]. Moreover, in comparison to fluorescence based sensors, only a limited number of absorbance-based visible polymeric sensors has been reported to date. More particularly, thermo or pH responsive polymeric sensors featuring a visible readout have largely focused upon solvatochromic dyes (e.g. mercocyanine, coumarin, rhodamine, dispersed red 1, bromothymol blue) that have been physically or covalently embedded into a thermoresponsive polymer matrix [25–32].

Recently, our group has reported a straightforward supramolecular approach to elaborate a new family of thermosensors with an associated direct visible readout [33]. This host-guest concept is based on the thermoresponsiveness of coloured complexes formed from naphthalene functionalized PNIPAM as guests and cyclobis(paraquat-*p*-phenylene) (**CBPQT**⁴⁺, **4Cl**[−]) as host. These systems above their cloud points undergo LCST-induced dethreading, thereby resulting in a complete disappearance of the characteristic purple colour associated with complexes of this type. This concept was notably exploited to create supramolecular-based programmable, reprogrammable thermometers that also display a thermal memory function. Here, we report on the elaboration of a new supramolecular polymeric system, consisting of a 1,5-diaminonaphthalene end functionalized PNIPAM (**Napht-N-PNIPAM**) complexed with **CBPQT**⁴⁺, **4Cl**[−], capable of sensing both temperature and pH with a visual readout. In this paper, the synthesis of **Napht-N-PNIPAM** and its propensity to form a strong coloured host-guest assembly in aqueous media with **CBPQT**⁴⁺, **4Cl**[−] is reported in detail, as well as the thermo and pH responsiveness of **Napht-N-PNIPAM-CBPQT** supramolecular complex.

2. Results & discussion

A novel RAFT agent **Napht-N-CTA** was conveniently prepared from the coupling reaction of 1,5-bis [2-(2-hydroxyethoxy)ethylamino]naphthalene [34] **1** and 2-(1-isobutyl)sulfanylthiocarbonylsulfanyl-2-methyl propionic acid (compound **2**, Scheme 1).

The structure of the **Napht-N-CTA** was confirmed by ¹H NMR, ¹³C NMR and 2D NMR (see ESI Figs. S1–S3 respectively) spectroscopies. ¹H NMR spectrum of **Napht-N-CTA** recorded in CD₃CN revealed the presence of the characteristic signals of protons belonging to the naphthalene unit ($\delta_{\text{H}_{2/6}} = \delta_{\text{H}_{3/7}} = 7.4$ ppm and $\delta_{\text{H}_{4/8}} = 6.9$ ppm) and the methyl fragment of the isobutyl group ($\delta_{\text{CH}_3} = 0.9$ ppm). Furthermore, the ¹³C spectrum clearly displayed chemical shifts at 172.1 ppm and 222.2 ppm ascribed to the amide carbonyl group and the thiocarbonyl fragment of the RAFT agent, respectively.

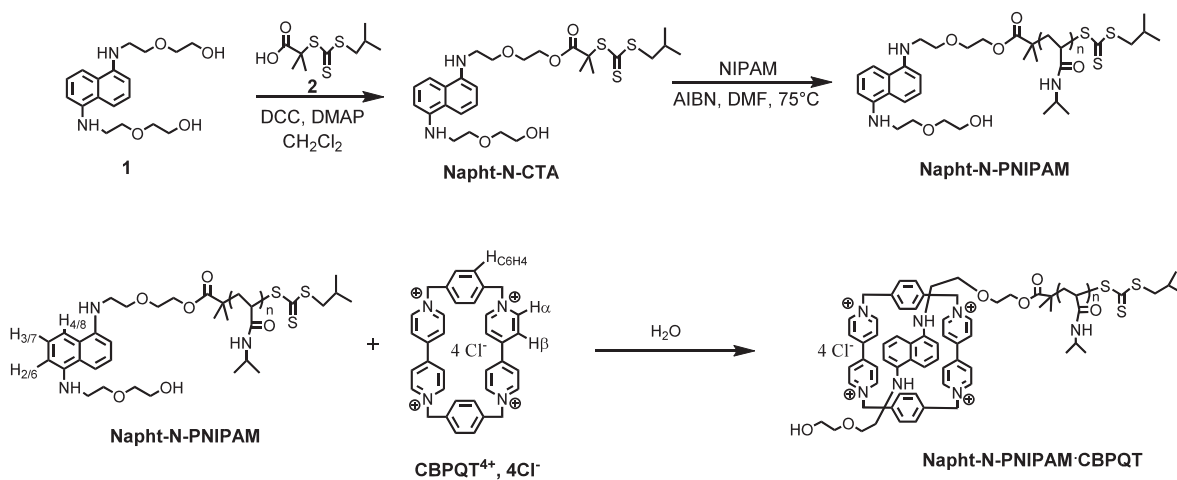
The ability of the **Napht-N-CTA** to promote RAFT polymerizations was demonstrated with *N*-isopropylacrylamide (NIPAM). The polymerization of NIPAM (150 equiv.) was carried out with azobis(isobutyronitrile) (AIBN, 0.2 equiv.) as a radical source and **Napht-N-CTA** (1 equiv.) in DMF at 75 °C for 1 h. The absolute molecular weight and the dispersity index (*D*) of the polymer were determined by SEC ($M_{\text{n,abs}} = 14,810$ g/mol, $\bar{D} = 1.07$, $dn/dc = 0.0886$ mL/g, Fig. S4). In addition, the structure of **Napht-N-PNIPAM** was confirmed by ¹H NMR spectroscopy in D₂O, which displayed the characteristic signals of PNIPAM ($\delta_{\text{N-CH}} = 3.95$ ppm, $\delta_{\text{CH}_3} = 1.20$ ppm, Fig. S5) in addition to those belonging to the naphthalene moiety ($\delta_{\text{H}_{2/6}} = \delta_{\text{H}_{3/7}} = 7.5$ ppm, $\delta_{\text{H}_{4/8}} = 6.9$ ppm, Fig. 1a).

Next, the ability of electron-rich **Napht-N-PNIPAM** to form a 1:1 complex with the electron-deficient **CBPQT**⁴⁺, **4Cl**[−] was investigated. The addition of aliquots of **CBPQT**⁴⁺, **4Cl**[−] to a solution of **Napht-N-PNIPAM** in water resulted in the immediate appearance of an intense blue-green colour, which is consistent with the formation of a donor-acceptor complex between the π -electron rich **Napht-N-PNIPAM** and the π -electron deficient **CBPQT**⁴⁺, **4Cl**[−]. This observation was confirmed by the appearance of a band centered at 697 nm in its UV-vis spectrum (Fig. 2a).

Next, we have studied the complex formation between **Napht-N-PNIPAM** and **CBPQT**⁴⁺, **4Cl**[−] in aqueous media by using NMR spectroscopy (¹H, 2D-ROESY, DOSY, COSY). The ¹H NMR spectrum of a 1:1 mixture **Napht-N-PNIPAM** and **CBPQT**⁴⁺, **4Cl**[−] revealed significant shifts for the H_β ($\Delta\delta = -0.96$ ppm), H_{C6H4} ($\Delta\delta = +0.31$ ppm) protons of **CBPQT**⁴⁺, **4Cl**[−] and H_{2/6}, H_{3/7} ($\Delta\delta = -1.38$ ppm), H_{4/8} ($\Delta\delta = -5.7$ ppm) of **Napht-N-PNIPAM** (Fig. 1b), that is in good agreement with previously reported data for complexes of this type. [34]

¹H NMR titration experiments were also carried out on **Napht-N-PNIPAM** upon adding aliquots of **CBPQT**⁴⁺, **4Cl**[−] (Fig. S6). ¹H NMR spectra clearly indicated the existence of the signal for uncomplexed H_{4/8} protons upon the addition of aliquots of **CBPQT**⁴⁺, **4Cl**[−], thereby suggesting a slow exchange at the NMR timescale between the uncomplexed (Fig. 1c) and complexed forms. Moreover, the ¹H NMR titration revealed the complete disappearance of the signal of uncomplexed H_{4/8} protons at 6.9 ppm when 1 equiv. of **CBPQT**⁴⁺, **4Cl**[−] was added, thus indicating the formation of a 1:1 complex between **Napht-N-PNIPAM** and **CBPQT**⁴⁺, **4Cl**[−]. Further proof regarding the formation of a pseudorotaxane architecture between **Napht-N-PNIPAM** and **CBPQT**⁴⁺, **4Cl**[−] was also obtained from its 2D ROESY spectrum that indeed displayed a dipolar correlation between H_{2/6}, H_{3/7} and H_{C6H4} protons belonging to the guest and host partners, respectively (Fig. 3a).

Next, to demonstrate the robustness of the host-guest interaction between **Napht-N-PNIPAM** and **CBPQT**⁴⁺, **4Cl**[−], two-dimensional diffusion ordered spectroscopy (DOSY) ¹H NMR spectroscopy and isothermal titration microcalorimetry (ITC) experiments were undertaken. 2D-DOSY ¹H NMR spectroscopy experiments showed for solutions of their individual components (**CBPQT**⁴⁺, **4Cl**[−] and **Napht-N-PNIPAM**) have a diffusion coefficient value of 1585 μm² s^{−1} and 73.3 μm² s^{−1}, respectively (Fig. 3b).



Scheme 1. Synthesis of the RAFT agent **Napht-N-CTA** and the polymer **Napht-N-PNIPAM**.

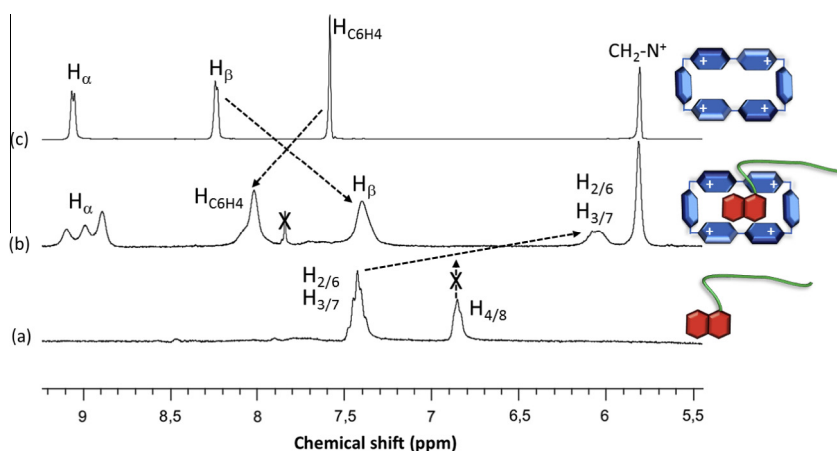


Fig. 1. Partial ^1H NMR spectra of: (a) **Napht-N-PNIPAM**, (b) **Napht-N-PNIPAM-CBPQT** and (c) **CBPQT $^{4+}$, 4Cl $^-$** . Recorded at 18 °C in D_2O .

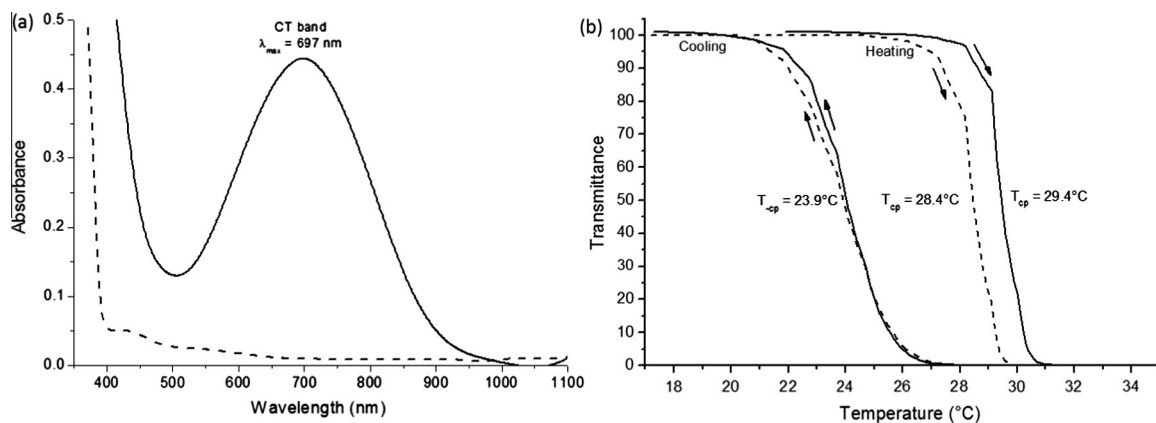


Fig. 2. UV-vis spectra (a) and thermo-sensitive phase transition recorded at 950 nm (b) of **Napht-N-PNIPAM** (---) and **Napht-N-PNIPAM** in presence of 1 equivalent of **CBPQT $^{4+}$** (-).

When DOSY experiments were undertaken on 1:1 **Napht-N-PNIPAM-CBPQT** solution of the complex, the protons belonging to **CBPQT $^{4+}$, 4Cl $^-$** moved to a lower and identical

diffusion coefficient to that of **Napht-N-PNIPAM** ($73.3 \mu\text{m}^2 \text{s}^{-1}$). Moreover, no signals for the free **CBPQT $^{4+}$, 4Cl $^-$** were observed, thus confirming the efficiency of the

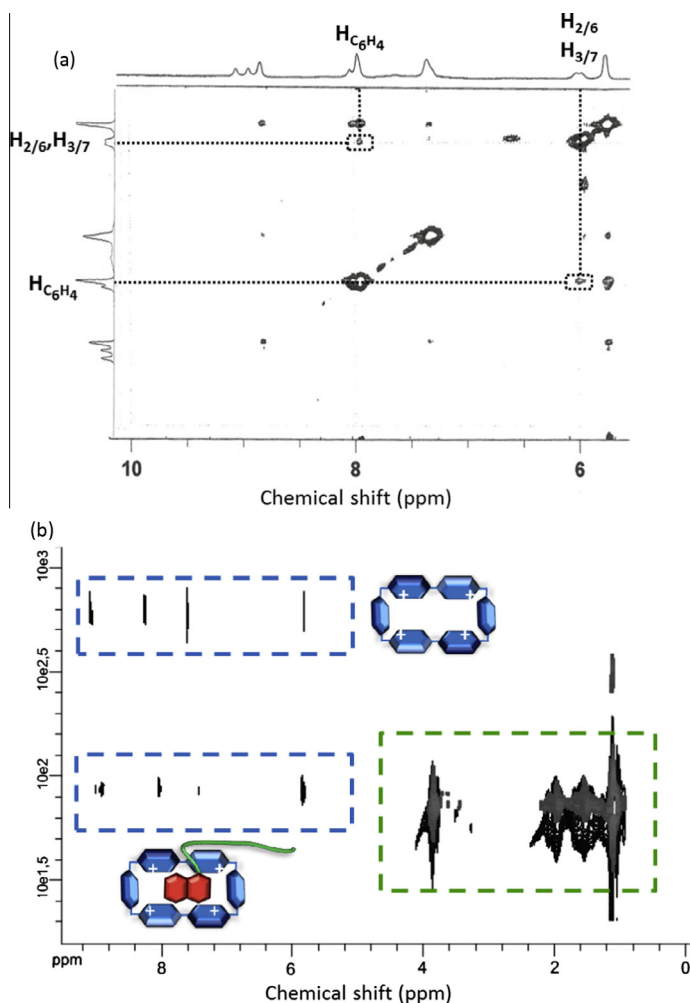


Fig. 3. (a) 2D-ROESY ^1H - ^1H spectrum (D_2O) of **Napht-N-PNIPAM-CBPQT**, (b) Superimposed ^1H NMR DOSY (D_2O) experiments of free **CBPQT $^{4+}$** , **4Cl $^-$** (upper black spectrum), **Napht-N-PNIPAM** (grey spectrum) and the 1:1 complex **Napht-N-PNIPAM-CBPQT** (bottom black spectrum).

coupling between **CBPQT $^{4+}$** , **4Cl $^-$** and **Napht-N-PNIPAM**. In addition, ITC experiments indicated that addition of aliquots of **CBPQT $^{4+}$** , **4Cl $^-$** to a dilute solution of **Napht-N-PNIPAM** in water gave rise to a large exothermic response ($\Delta H = -46.08 (\pm 0.26)$ kcal/mol) in good agreement with the relatively large estimated association constant of $K_a = 9.2 (\pm 0.7) \times 10^4 \text{ M}^{-1}$ (Fig. S7).

2.1. Thermo-responsiveness of **Napht-N-PNIPAM-CBPQT** complex in water

The thermo-responsiveness of the **Napht-N-PNIPAM-CBPQT** complex was first investigated by turbidity measurements using UV-vis spectroscopy (Fig. 2b). The cloud point of the polymer complexed with **CBPQT $^{4+}$** , **4Cl $^-$** in water was determined as 29.4 °C from the midpoint of the transmittance value (Fig. 2b). This value was slightly higher than the cloud point estimated for **Napht-N-PNIPAM** ($T_{cp} = 28.4$ °C, Fig. 2b), thereby indicating that the hydrophilicity-hydrophobicity balance of the material can be displaced towards a more hydrophilic structure by

masking the hydrophobicity of the naphthalene unit through the formation of a pseudorotaxane-like architecture with the more hydrophilic **CBPQT $^{4+}$** , **4Cl $^-$** host [10]. More interestingly, despite the high K_a value, the phase transition of the complex ($T > T_{cp}$) induced a complete disappearance of the green-blue colour of the aqueous solution, suggesting a disruption of the complex upon crossing the T_{cp} . This was also evidenced by the fact that the UV-vis spectra of **Napht-N-PNIPAM** and **Napht-N-PNIPAM-CBPQT**, **4Cl $^-$** were quite similar upon cooling the samples (Fig. 2b). To get further insight on the cloud point-mediated host-guest disassembly, variable temperature ^1H NMR spectroscopy experiments were carried out. More particularly, we have investigated the changes in the ^1H NMR spectra of **Napht-N-PNIPAM-CBPQT** complex upon cycling the temperature between 18 °C ($T < T_{cp}$) and 35 °C ($T > T_{cp}$) in D_2O . As expected, the ^1H NMR spectra of **Napht-N-PNIPAM-CBPQT** upon heating from 18 °C (Fig. 4a) to 35 °C (Fig. 4b) revealed a complete disappearance of the protons belonging to the polymer due to the precipitation of the polymer at 35 °C ($T > T_{cp}$). Moreover,

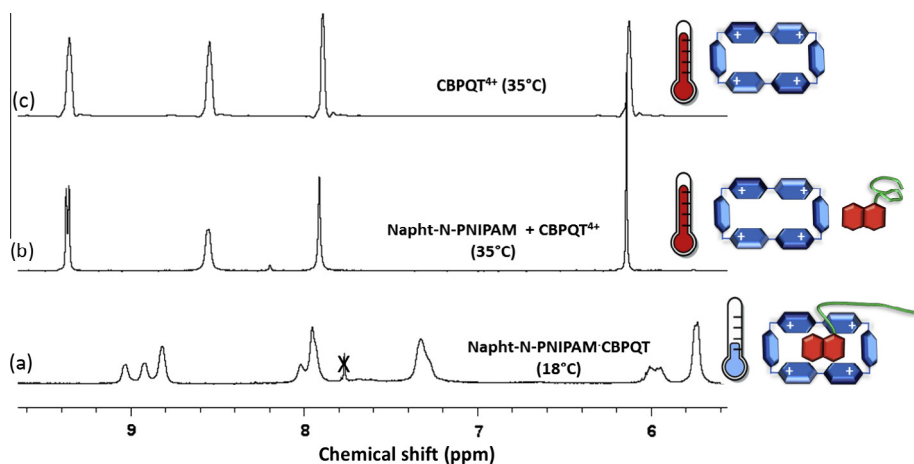


Fig. 4. Partial ^1H NMR spectra (D_2O) of **Napht-N-PNIPAM-CBPQT** at (a) 18 °C, (b) 35 °C and (c) **CBPQT $^{4+}$** , **4Cl $^-$** at 35 °C.

the signals recorded at 35 °C shown in Fig. 4b perfectly fit to the signal of the protons of uncomplexed **CBPQT $^{4+}$** (Fig. 4c), clearly suggesting that the dethreading of the complexation occurred upon heating the complex over the cloud point. In addition, when the temperature was cooled below the cloud point, the colour of the solution turned back to intense blue-green. This feature was monitored by UV-vis spectroscopy and it appeared that the maximum of absorbance of the absorption at 697 nm did not change even after 3 cycles of heating/cooling, suggesting that the complexation/dethreading upon simply heating and cooling the aqueous solution is reversible (Fig. S8).

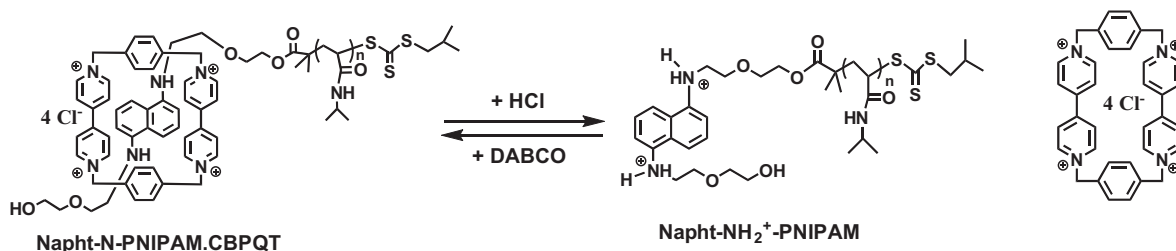
2.2. pH-responsiveness of **Napht-N-PNIPAM-CBPQT** complex in water

After demonstrating the thermo-sensitivity of **Napht-N-PNIPAM-CBPQT**, its pH-responsiveness was next studied (Scheme 2). Here, the main objective was to exploit the propensity of the diamionaphthalene unit located on PNIPAM to become protonated in acidic environments, thus affording the corresponding **Napht-NH $_2^+$ -PNIPAM** to promote the dethreading of the pseudorotaxane architecture through Coulombic repulsion. Upon the addition of aliquots of aqueous HCl to a solution containing the **Napht-N-PNIPAM-CBPQT** complex, the intense green colour ($\lambda_{\text{max}} = 697$ nm) disappeared rapidly and a colourless solution was observed as shown in Fig. 5. The UV spectrum upon adding HCl was almost identical to that of the

uncomplexed polymer. Moreover, the reversibility of the procedure was demonstrated by adding aliquots of aqueous basic solution of 1,4-diazabicyclo[2.2.2] octane (DABCO, 1.5 M in H_2O) until pH = 7 was reached. In this way, the colour of the solution turned from colourless to intense blue-green and the obtained UV spectrum showed the characteristic band at 697 nm (Fig. S9). It is noteworthy that performing 3 complete cycles of pH = 1/pH = 7 switching provided evidence for successive decomplexation/complexation (Fig. S9).

In addition to UV-vis investigations, ^1H NMR spectroscopy experiments were performed to corroborate optical studies in acidic medium. As shown in Fig. 6, when aliquots of DCl (35 wt% in D_2O) were added to the **Napht-N-PNIPAM-CBPQT $^{4+}$** complex (spectrum b), signals corresponding to the protons of uncomplexed **CBPQT $^{4+}$** , **4Cl $^-$** were observed (*i.e.* H_α , H_β , H_{C6H4}), indicating that the protonation of the naphthalene unit efficiently led to the disruption of the host/guest complex upon decreasing the pH of the solution.

The reversibility of the procedure was demonstrated by adding aliquots of an aqueous solution of DABCO (1.5 M in D_2O) until pH = 7 was reached. As stated previously, the colour of the solution turned intense blue-green when the pH was adjusted to 7. In the ^1H NMR spectrum (Fig. S10), the signals of the protons of free **CBPQT $^{4+}$** disappeared while characteristic signals resulting from host-guest complexation appeared. Moreover, the reversibility of the procedure was demonstrated by performing 3



Scheme 2. Study of the pH-responsiveness of **Napht-N-PNIPAM**.

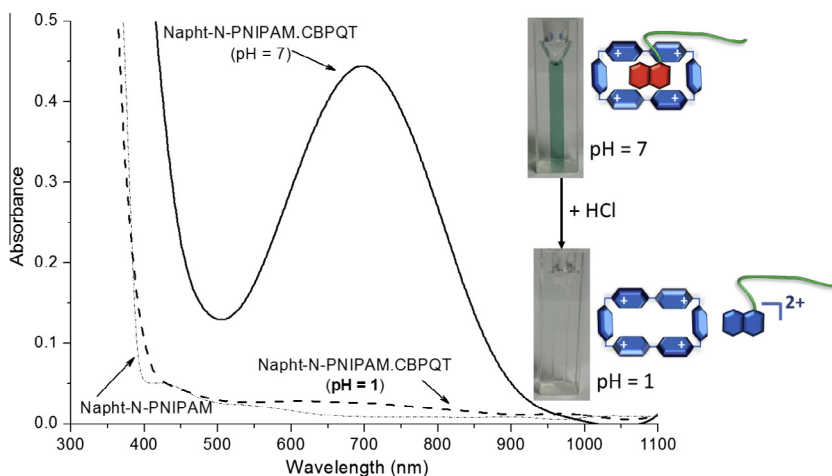


Fig. 5. UV–vis spectra of uncomplexed **Napht-N-PNIPAM** and **Napht-N-PNIPAM** in presence of 1 equiv. of **CBPQT⁴⁺**, **4Cl⁻** at pH = 1 and pH = 7.

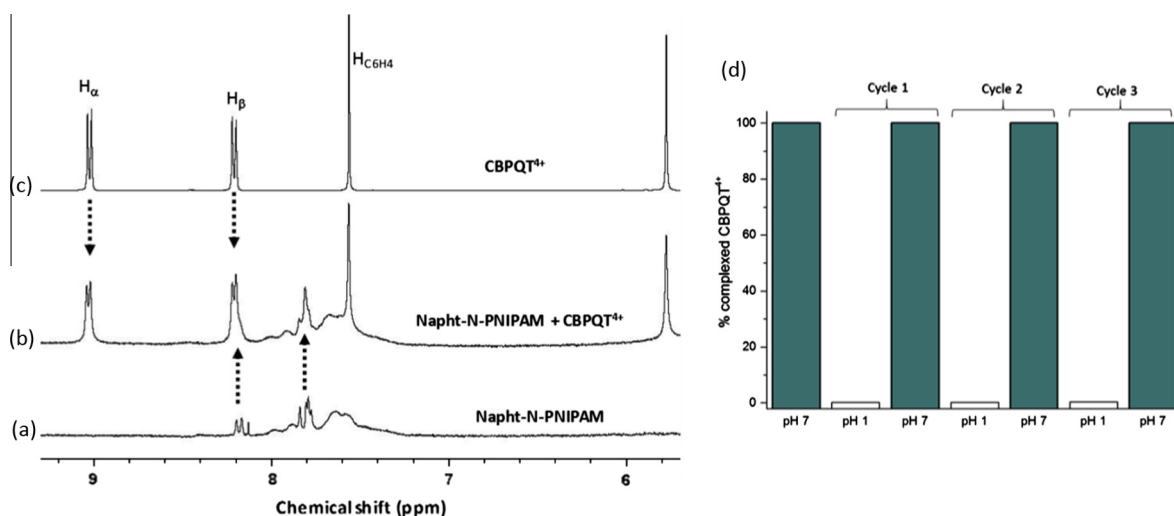


Fig. 6. Partial ^1H NMR spectra (35 wt% DCl in D_2O) of (a) **Napht-NH₂-PNIPAM**, (b) polymer complex in acidic medium and (c) **CBPQT⁴⁺**, **4Cl⁻**. Chart (d) represents the reversibility of pH = 7/pH = 1 switching process upon the addition of DCl (35 wt% in D_2O) and DABCO (1.5 M in D_2O) showing the complexation/dethreading phenomena.

complete pH = 1/pH = 7 cycles by simply adding aliquots of solutions of DCl and DABCO, respectively (Fig. 6d). The resulting ^1H NMR spectra (Fig. S10) clearly demonstrate the reversibility of the experiment and the stability of the species after several cycles.

3. Conclusion

In this contribution, we have synthesized, using a RAFT procedure, a novel well-defined thermoresponsive polymer (**Napht-N-PNIPAM**) bearing a pH-sensitive 1,5-diaminonaphthalene moiety. We have demonstrated its ability to form a strong coloured **Napht-N-PNIPAM.CBPQT** based pseudorotaxane-like architecture in water with **CBPQT⁴⁺**, **4Cl⁻** by performing ^1H NMR spectroscopy, ITC and UV–Vis measurements. Interestingly, this

complex can be conveniently disassembled either beyond its cloud point or in acidic conditions, thereby leading in both cases to the visual disappearance of the intense blue-green solution. Hence, such supramolecular assemblies can be considered as a dual sensor capable of sensing both temperature and pH with a direct visible readout. Based on this supramolecular approach, we are currently designing more sophisticated multifunctional sensors capable of monitoring temperature, pH and CO_2 . Our work in this area will be reported in due course.

Acknowledgments

P.W. gratefully acknowledges financial support from the Agence Nationale de la Recherche (STRAPA project, ANR-12-BS08-0005). GC thanks the EPSRC for funding

(EP/E036244). The authors would thank Marc Bria for his help and fruitful discussions about NMR experiments.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.eurpolymj.2015.02.033>.

References

- [1] Mendes PM. Stimuli-responsive surfaces for bio-applications. *Chem Soc Rev* 2008;37(11):2512–29.
- [2] Roy D, Cambre JN, Sumerlin BS. Future perspectives and recent advances in stimuli-responsive materials. *Prog Polym Sci* 2010;35(1–2):278–301.
- [3] Liu F, Urban MW. Recent advances and challenges in designing stimuli-responsive polymers. *Prog Polym Sci* 2010;35(1–2):3–23.
- [4] Hoffman AS. Stimuli-responsive polymers: Biomedical applications and challenges for clinical translation. *Adv Drug Delivery Rev* 2013;65(1):10–6.
- [5] Zhuang J, Gordon MR, Ventura J, Li L, Thayumanavan S. Multi-stimuli responsive macromolecules and their assemblies. *Chem Soc Rev* 2013;42(17):7421–35.
- [6] Schattling P, Jochum FD, Theato P. Multi-stimuli responsive polymers - the all-in-one talents. *Polym Chem* 2014;5(1):25–36.
- [7] Cooke G, Garety JF, Hewage SG, Jordan BJ, Rabani G, Rotello VM, et al. Tuneable side-chain supramolecular polymer. *Org Lett* 2007;9(3):481–4.
- [8] Bigot J, Bria M, Caldwell ST, Cazaux F, Cooper A, Charleux B, et al. LCST: a powerful tool to control complexation between a dialkoxynaphthalene-functionalised poly(N-isopropylacrylamide) and **CBPQT**⁴⁺ in water. *Chem Commun* 2009;35:5266–8.
- [9] Stuart MAC, Huck WTS, Genzer J, Muller M, Ober C, Stamm M, et al. Emerging applications of stimuli-responsive polymer materials. *Nat Mater* 2010;9(2):101–13.
- [10] Sambe L, Stoffelbach F, Lyskawa J, Delattre F, Fournier D, Bouteiller L, et al. Host-guest modulation of the micellization of a tetrathiafulvalene-functionalized poly(n-isopropylacrylamide). *Macromolecules* 2011;44(16):6532–8.
- [11] Cabane E, Zhang X, Langowska K, Palivan CG, Meier W. Stimuli-responsive polymers and their applications in nanomedicine. *Biointerphases* 2012;7(1):1–27.
- [12] Kelley EG, Albert JNL, Sullivan MO, Epps III TH. Stimuli-responsive copolymer solution and surface assemblies for biomedical applications. *Chem Soc Rev* 2013;42(17):7057–71.
- [13] Ge Z, Liu S. Functional block copolymer assemblies responsive to tumor and intracellular microenvironments for site-specific drug delivery and enhanced imaging performance. *Chem Soc Rev* 2013;42(17):7289–325.
- [14] Doring A, Birnbaum W, Kuckling D. Responsive hydrogels – structurally and dimensionally optimized smart frameworks for applications in catalysis, micro-system technology and material science. *Chem Soc Rev* 2013;42(17):7391–420.
- [15] Klaiherd A, Nagamani C, Thayumanavan S. Multi-stimuli sensitive amphiphilic block copolymer assemblies. *J Am Chem Soc* 2009;131(13):4830–8.
- [16] Motorov M, Roiter Y, Tokarev I, Minko S. Stimuli-responsive nanoparticles, nanogels and capsules for integrated multifunctional intelligent systems. *Prog Polym Sci* 2010;35(1–2):174–211.
- [17] Mura S, Nicolas J, Couvreur P. Stimuli-responsive nanocarriers for drug delivery. *Nat Mater* 2013;12(11):991–1003.
- [18] Gota C, Uchiyama S, Ohwada T. Accurate fluorescent polymeric thermometers containing an ionic component. *Analyst* 2007;132(2):121–6.
- [19] Shiraishi Y, Miyamoto R, Hirai T. A hemicyanine-conjugated copolymer as a highly sensitive fluorescent thermometer. *Langmuir* 2008;24(8):4273–9.
- [20] Pietsch C, Vollrath A, Hoogenboom R, Schubert US. A fluorescent thermometer based on a pyrene-labeled thermoresponsive polymer. *Sensors* 2010;10(9):7979–90.
- [21] Pietsch C, Schubert US, Hoogenboom R. Aqueous polymeric sensors based on temperature-induced polymer phase transitions and solvatochromic dyes. *Chem Commun* 2011;47(31):8750–65.
- [22] Okabe K, Inada N, Gota C, Harada Y, Funatsu T, Uchiyama S. Intracellular temperature mapping with a fluorescent polymeric thermometer and fluorescence lifetime imaging microscopy. *Nat Commun* 2012;3:1–9.
- [23] Wang X-d, Wolfbeis OS, Meier RJ. Luminescent probes and sensors for temperature. *Chem Soc Rev* 2013;42(19):7834–69.
- [24] Tsuji T, Yoshida S, Yoshida A, Uchiyama S. Cationic fluorescent polymeric thermometers with the ability to enter yeast and mammalian cells for practical intracellular temperature measurements. *Anal Chem* 2013;85(20):9815–23.
- [25] Pietsch C, Hoogenboom R, Schubert US. Soluble polymeric dual sensor for temperature and pH value. *Angew Chem* 2009;48(31):5653–6.
- [26] Hong SW, Ahn C-H, Huh J, Jo WH. Synthesis of a PEGylated polymeric pH sensor and its pH sensitivity by fluorescence resonance energy transfer. *Macromolecules* 2006;39(22):7694–700.
- [27] Bryleva EY, Vodolazkaya NA, McHedlov-Petrosyan NO, Samokhina LV, Matveevskaya NA, Tolmachev AV. Interfacial properties of cetyltrimethylammonium-coated SiO₂ nanoparticles in aqueous media as studied by using different indicator dyes. *J Colloid Interface Sci* 2007;316(2):712–22.
- [28] Koopmans C, Ritter H. Color change of N-isopropylacrylamide copolymer bearing reichardt's dye as optical sensor for lower critical solution temperature and for host-guest interaction with β -cyclodextrin. *J Am Chem Soc* 2007;129(12):3502–3.
- [29] Wu W, Zhou T, Aiello M, Zhou S. Optically pH and H₂O₂ dual responsive composite colloids through the directed assembly of organic dyes on responsive microgels. *Chem Mater* 2009;21(20):4905–13.
- [30] Peng H-s, Stolwijk JA, Sun L-N, Wegener J, Wolfbeis OS. A nanogel for ratiometric fluorescent sensing of intracellular pH values. *Angew Chem* 2010;49(25):4246–9.
- [31] Li C, Zhang Y, Hu J, Cheng J, Liu S. Reversible three-state switching of multicolor fluorescence emission by multiple stimuli modulated FRET processes within thermoresponsive polymeric micelles. *Angew Chem* 2010;49(30):5120–4.
- [32] Pietsch C, Hoogenboom R, Schubert US. PMMA based soluble polymeric temperature sensors based on UCST transition and solvatochromic dyes. *Polym Chem* 2010;1(7):1005–8.
- [33] Sambe L, de La Rosa VR, Belal K, Stoffelbach F, Lyskawa J, Delattre F, et al. Programmable polymer-based supramolecular temperature sensor with a memory function. *Angew Chem* 2014;53(20):5044–8.
- [34] Sue C-H, Basu S, Fahrenbach AC, Shveyd AK, Dey SK, Botros YY, et al. Enabling tetracationic cyclophane production by trading templates. *Chem Sci* 2010;1(1):119–25.