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**Supramolecular control over pH- and temperature-responsive
dialkoxynaphthalene-functionalized poly(2-(dimethylamino)ethyl
methacrylate) in water**

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Abstract

In the framework of the development of multi-responsive polymer materials, a well-defined copolymer bearing supramolecular recognition units was designed based on 2-(dimethylamino)ethyl methacrylate (DMAEMA) and a dialkoxynaphthalene-functionalized monomer (NaphtA). The supramolecular host-guest interactions of this P(DMAEMA-*co*-NaphtA) copolymer with the electron-deficient CBPQT⁴⁺, 4 Cl⁻ cyclophane host were studied by ¹H NMR spectroscopy, UV-Visible spectroscopy and isothermal titration calorimetry (ITC), revealing, a high association constant of $6.5 \times 10^5 \text{ M}^{-1}$ in water. The addition of CBPQT⁴⁺, 4 Cl⁻ to a colorless solution of the copolymer in water resulted in a purple solution due to the formation of donor-acceptor inclusion complexes, the intensity being directly proportional to the amount of host added. Investigations on the thermoresponsive behavior of the naphthalene-

functionalized copolymer highlighted that the cloud point temperature is directly proportional to the amount of CBPQT⁴⁺, 4 Cl⁻ host added and can simply be programmed within a temperature window from 30 °C to 48 °C by playing with pH. The dethreading process was studied as function of temperature and anionic exchange of the counterions of the CBPQT⁴⁺, 4Cl⁻. Interestingly, a partial decomplexation was observed by heating the sample above the cloud point temperature while a complete and programmable dethreading was achieved by adding the anionic surfactant sodium dodecyl sulfate (SDS) as a competitive counterion of the host molecule.

Introduction

Over the last decades, synthetic supramolecular chemistry, based on non-covalent interactions, has been employed with the final aim of designing systems with an advanced degree of complexity, beyond the individual molecules, comparable to those responsible for the origin of life.^{1, 2} For this purpose, the design of a myriad of macrocyclic receptors^{3, 4} for host-guest chemistry has offered a way to fine-tune affinity and selectivity in molecular recognition and to construct materials by a bottom-up molecular approach.^{5, 6} The control over the complexation/decomplexation phenomena of such host-guest complexes in aqueous media is essential for the regulation of their behavior and corresponding properties.⁷ In this context, several strategies were developed to regulate the reversible binding of organic molecules, essentially based on modification of known macrocyclic hosts or guests to introduce stimuli-responsive switchability.⁸ However, the large majority of such systems undergo chemical changes upon exposure to stimulus and only a few enable switching while retaining their chemical integrity.⁸ The combination of thermo-responsive polymers and host-guest supramolecular chemistry allowed to control both the lower critical solution temperature (LCST) behavior of the polymer solutions as well as the complex disruption, while keeping the chemical properties of the supramolecular modules intact. Indeed, many studies have reported

the complexation of cyclodextrins (CDs) with side-chain or end-group guest-functionalized responsive polymers such as polyacrylamides⁹⁻¹³ and poly(2-oxazolines).¹⁴⁻¹⁶ The addition of CDs to guest-functionalized thermo-responsive polymers in water greatly affects their cloud point temperature (T_{CP}) due to the complexation of CDs with the guests, thereby shielding the hydrophobic guest molecules from water. Aside CDs, other hosts have also been used to tailor the phase transition of responsive polymers such as cucurbit[n]urils,^{14, 17} pillar[n]arenes^{18, 19} and cyclobis(paraquat-*p*-phenylene).²⁰⁻²² We previously showed that the formation of host-guest complexes of cyclophane cyclobis(paraquat-*p*-phenylene) (CBPQT⁴⁺ also named Blue Box) with side-chains dialkyloxynaphthalene-functionalized poly(*N*-isopropylacrylamide) (PNIPAm) polymer is accompanied by a non-linear increase of the T_{CP} of the polymer from 20 °C to 30 °C.²¹ Moreover, the coil-to-globule transition of the PNIPAm polymer was found to induce complete and reversible decomplexation of the CBPQT⁴⁺ host-guest complex with dialkyloxynaphthalene, which is accompanied by a change in color as visual read-out.^{20, 21} However, these previously reported stimuli-responsive host-guest systems simply respond to isolated and independent external triggers. As a result, in the quest of mimicking biological systems, a remaining challenge concerns the development of supramolecular host-guest systems that are able to finely respond to multiple and dependent environmental changes. For this purpose, we recently designed a dialkyloxynaphthalene-end functionalized copolymer of NIPAm and ionisable acrylic acid (AA) units, which combined both temperature and pH-responsiveness.²³ By increasing the pH from 1 to 5, the deprotonation of the AA units was accompanied by a drastic increase in polymer hydrophilicity and a decrease in temperature-triggered CBPQT⁴⁺ release. Nevertheless, the T_{CP} value was difficult to adjust by the pH, since a slight increase in pH around the pK_a of the AA units, from 4 to 5, led to a large rise in T_{CP} from 32 °C to 52 °C.²³ In this context, poly(2-(dimethylamino)ethyl methacrylate) (PDMAEMA) exhibits interesting features,²⁴⁻²⁹ such as a T_{CP} that depends on the molar mass,

its composition and the pH due to the ionizable tertiary amine moieties on the polymer backbone with a pK_a in between 7.0 and 7.5.²⁹⁻³¹ Therefore, the T_{CP} of PDMAEMA can be increased under more acidic condition due to protonation of the tertiary amine group and lowered under basic condition due to deprotonation of the tertiary amine group.

In this work, we report on the Reversible Addition-Fragmentation chain Transfer (RAFT) copolymerization of DMAEMA with a hydrophobic dialkoxynaphthalene-functionalized monomer to prepare a well-defined copolymer bearing electron-rich pendant naphthalene guest units, anticipated to lead to a multiresponsive supramolecular system in presence of CBPQT⁴⁺. The thermo- and pH responsiveness of the guest functionalized PDMAEMA-based copolymer was evaluated through the determination of the T_{CP} of the copolymer upon sequential addition of the CBPQT⁴⁺, 4 Cl⁻ host and at different pH values. In addition, the dethreading process of the supramolecular polymer materials was studied by heating the samples over their T_{CP} and as well as by addition of a competitive hydrophobic counterion to replace the chloride atoms.

Experimental section

Materials. All reagents were purchased from Sigma-Aldrich and used without further purification, unless otherwise noted. The monomer 2-(Dimethylamino)ethyl methacrylate (DMAEMA) was purified on an aluminium oxide column. Azobis(isobutyronitrile) (AIBN) was recrystallized from hexane. Cyclobis(paraquat-*p*-phenylene) (CBPQT⁴⁺, 4 Cl⁻) was synthesized according to literature procedures.³² The original synthesis and characterization of the 1-[2-(2-hydroxyethoxy)ethoxy]-5-[2-(2-methoxyethoxy)ethoxy]naphthalene (NaphtA) monomer (**Figure S1** and **Figure S2**) are reported in Supporting Informations.

RAFT copolymerization of NaphtA and DMAEMA. In a Schlenk flask, DMAEMA (1.9 g, 12 mmol, 95 eq), NaphtA (271 mg, 0.635 mmol, 5 eq), 2-cyano-2-propyl benzodithioate

(CPDB) (28 mg, 0.127 mmol, 1 eq) and AIBN (4.1 mg, 25.4 μmol , 0.2 eq) were solubilized with 5 mL of freshly distilled toluene. Three freeze-pump-thaw cycles were performed before heating the mixture at 90 °C. After 6 h of polymerization, the solution was immediately cooled down by immersing the reaction flask into liquid nitrogen. The copolymer was recovered by 2 successive precipitations from toluene in petroleum ether and then dried overnight under vacuum at room temperature. An overall conversion of 70 % (determined by ^1H NMR spectroscopy) and an absolute number-average molar mass of 10,900 $\text{g}\cdot\text{mol}^{-1}$ with a dispersity (D) of 1.18 (determined by SEC in THF, $\text{dn/dc} = 0.1043 \text{ mL}\cdot\text{g}^{-1}$) were obtained.

Analytical techniques. ^1H NMR spectra were recorded on a Bruker 300 MHz FT-NMR spectrometer and chemical shifts (δ) are given in ppm. Size exclusion chromatography (SEC) analyses were performed on a Waters system equipped with three columns (Styragel HR1, Styragel HR3, Styragel HR4) placed in series and coupled with two Wyatt detectors: a differential refractive index (RI) detector, and a Multi-Angle Light Scattering (MALS) detector (laser $\lambda = 670 \text{ nm}$). THF was used as eluent with a flow rate of 1 $\text{mL}\cdot\text{min}^{-1}$. Isothermal titration calorimetry (ITC) experiments were performed at 25 °C using a MicroCal VP-ITC titration microcalorimeter (MicroCal, Northampton, MA, USA) with a sample cell volume of 1.4 mL, and a stirring of 400 rpm, following standard procedures. The copolymer was dissolved in deionised water and the solution degassed gently under vacuum before use. The titration consisted in an initial 2 μl pre-injection followed by 24 injections (10 μL each) of a solution of CBPQT^{4+} , 4 Cl^- (10 $\text{mmol}\cdot\text{L}^{-1}$) into the solution of P(DMAEMA-*co*-NaphtA) copolymer (0.292 $\text{mmol}\cdot\text{L}^{-1}$). Control experiments with identical injections of CBPQT^{4+} , 4 Cl^- into water were used for baseline correction of the titration data. The T_{CP} of P(DMAEMA-*co*-NaphtA) copolymer solutions in deionized water at 5 $\text{g}\cdot\text{L}^{-1}$ were determined by turbidity measurements at different pH values. The pH of freshly prepared solution was 9.5 and was decreased by bubbling CO_2 into the solutions till 9 and to 8.5. A Cary 3500 Scan UV-Visible spectrometer

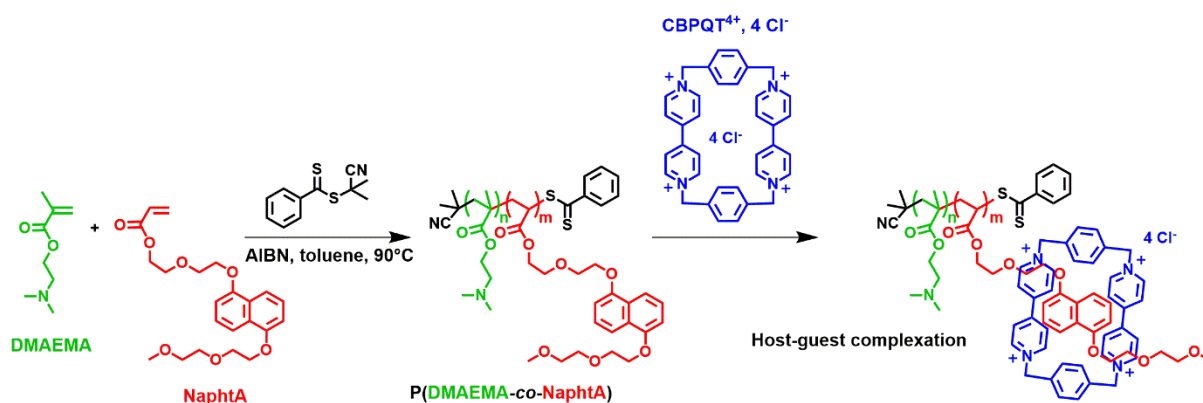
equipped with a multicell Peltier temperature controller was used. The heating rate was 1 °C.min⁻¹ and the transmittance was measured at 800 nm, wavelength at which clear solutions do not absorb. T_{CP} is defined during the heating as the temperature corresponding to a transmittance of 50%.

Titration of the copolymer by UV-Visible spectroscopy. Aliquots of an aqueous solution of CBPQT⁴⁺, 4 Cl⁻ (0.151 mol.L⁻¹, 9 μL per equivalent) from 1 to 10 equivalents were added to a solution of P(DMAEMA-*co*-NaphtA) copolymer (3 mL, 5g.L⁻¹, 6.9×10⁻⁶ mol of naphthalene units). The association constant K_a for the 1:1 complexes between the CBPQT⁴⁺, 4 Cl⁻ hosts and the naphthalene-based guest units was obtained by plotting the absorbance at 520 nm, corresponding to the charge transfer band of the complexes, as a function of the molar concentration of CBPQT⁴⁺, 4 Cl⁻ host added. The data collected were fitted by a non-linear regression (**Figure S3**) as reported in the literature.^{33, 34} Aliquots of sodium dodecyl sulfate (SDS, 0.69 mol.L⁻¹) were added to the final solution, 4 equivalents of SDS are needed to exchange the four chloride counter anions of 1 equivalent of CBPQT⁴⁺, 4 Cl⁻. After adding each aliquot of SDS, the sample was filtered before prior to analysis by UV-Visible spectroscopy.

Titration of the copolymer by ¹H NMR spectroscopy. In a NMR tube, 16 mg of P(DMAEMA-*co*-NaphtA) copolymer were solubilized in 0.5 mL of D₂O. Aliquots of a CBPQT⁴⁺, 4 Cl⁻ solution (95.9 mmol.L⁻¹) were successively added to reach 10 equivalents. Experiments were run at 20 °C and 70 °C.

Results and Discussion

Synthesis of P(DMAEMA-*co*-NaphtA) copolymer. The RAFT copolymerization of DMAEMA (95 eq.) and NaphtA (5 eq.) was carried out with azobis(isobutyronitrile) (AIBN, 0.2 eq) as radical source and 2-cyano-2-propyl benzodithioate (CPDB, 1 eq) as chain transfer agent (CTA) in toluene at 90 °C (**Scheme 1**).



Scheme 1. Synthesis of P(DMAEMA-*co*-NaphtA) copolymer by RAFT polymerization and its subsequent complexation with CBPQT⁴⁺, 4 Cl⁻.

After purification, the absolute number-average molar mass ($\overline{M}_{n,abs}$) and the dispersity (\mathcal{D}) of the copolymer were determined by SEC ($\overline{M}_{n,abs} = 10,900 \text{ g}\cdot\text{mol}^{-1}$, $\mathcal{D} = 1.18$). The structure of P(DMAEMA-*co*-NaphtA) was confirmed by ¹H NMR spectroscopy. The fully assigned spectrum (**Figure 1**), displayed the characteristic resonance signals of NaphtA ($H_{2/6} = 7.0 \text{ ppm}$, $H_{3/7} = 7.4 \text{ ppm}$, $H_{4/8} = 7.8 \text{ ppm}$) and DMAEMA units ($H_g = 2.6 \text{ ppm}$, $H_h = 2.3 \text{ ppm}$). The degree of polymerization and the molar composition of the copolymer were calculated using the integration of the signals of the protons of the CTA (7.5, 7.6 and 7.9 ppm) and those belonging to the monomer units. The resulting copolymer is composed of 8.3 mol% of NaphtA and 91.7 mol% of DMAEMA, representing an average number of units per chain of 58 for DMAEMA and 5 for NaphtA, and consequently a \overline{M}_n value of $10,650 \text{ g}\cdot\text{mol}^{-1}$, in accordance with the value determined by SEC.

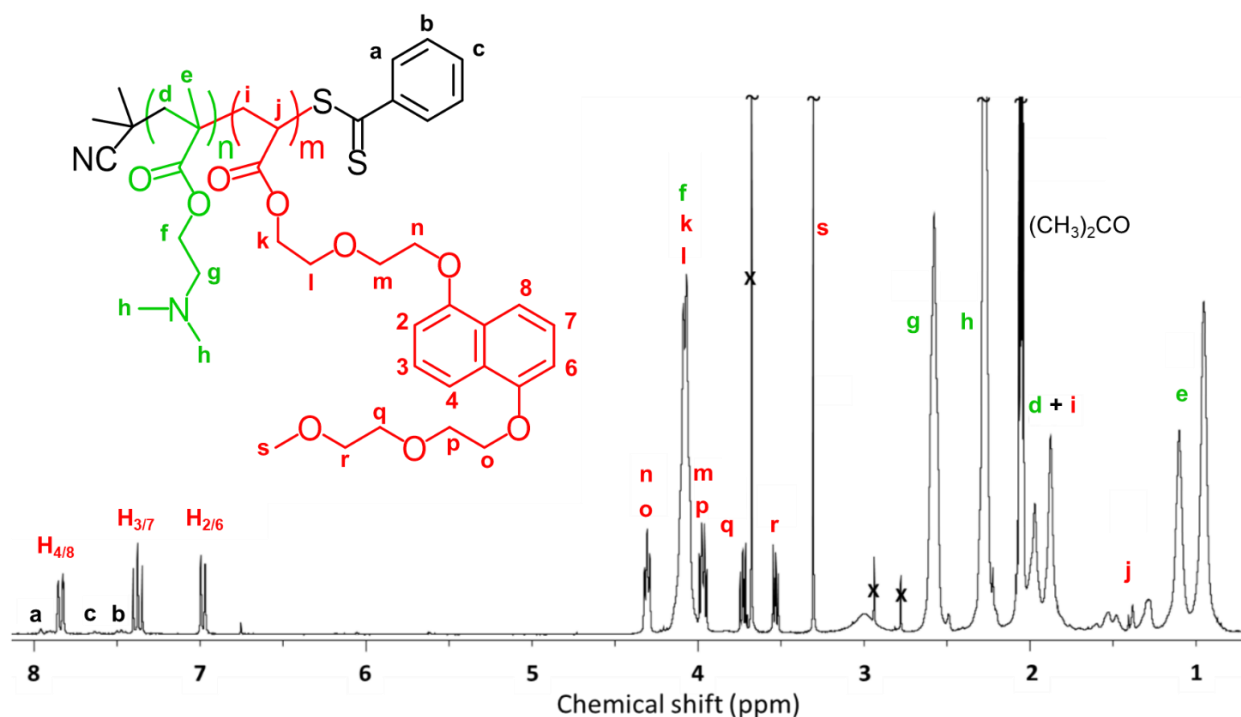


Figure 1. ^1H NMR spectrum of P(DMAEMA-*co*-NaphtA) in acetone- d_6 .

Host-guest complexation studies. The ability of the electron-rich naphthalene derivative units in the P(DMAEMA-*co*-NaphtA) copolymer to form host-guest complexes with the electron-deficient CBPQT $^{4+}$, 4 Cl $^-$ in water was first investigated by UV-Visible spectroscopy. Successive additions of aliquots of CBPQT $^{4+}$, 4 Cl $^-$ (from 1 to 10 equivalents relative to naphthalene units) to a colorless aqueous solution of P(DMAEMA-*co*-NaphtA), resulted in the appearance of a purple color consistent with the formation of this donor-acceptor complex. This observation was confirmed by the appearance of an absorption band centered at 520 nm in the UV-visible spectra (**Figure 2A**). Interestingly, the relative absorbance at 520 nm linearly increases with the molar ratio of CBPQT $^{4+}$, 4 Cl $^-$ to 5 equivalents before reaching a plateau after the addition of the sixth equivalent. This result is consistent with the composition previously determined by ^1H NMR spectroscopy (**Figure 1**) and corresponds to the expected complex

stoichiometry of one CBPQT⁴⁺, 4 Cl⁻ per naphthalene unit. A high association constant (K_a) of $1.74 \times 10^5 \text{ M}^{-1}$ was determined by fitting the data using a non-linear regression.

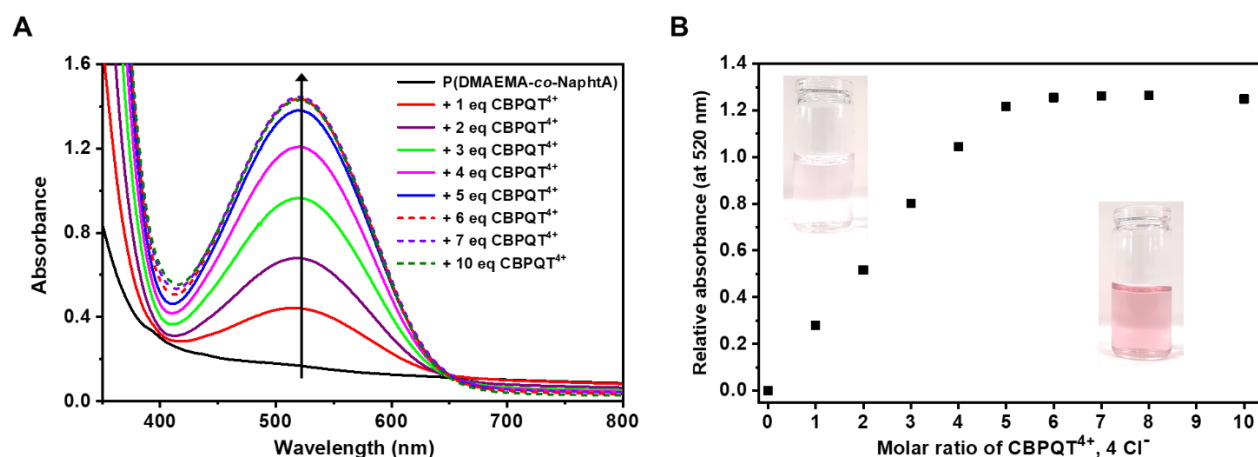


Figure 2. A) UV-Visible spectra of a P(DMAEMA-*co*-NaphtA) aqueous solution (5 g.L^{-1}) upon addition of aliquots of a concentrated solution of CBPQT⁴⁺, 4 Cl⁻ (from 1 to 10 equivalents). B) Dependence of the absorbance at 520 nm *versus* molar ratio of CBPQT⁴⁺, 4 Cl⁻ added. Picture insets represent the copolymer solution before the addition of CBPQT⁴⁺, 4 Cl⁻ (top, colorless solution) and the copolymer solution with 5 equivalents of CBPQT⁴⁺, 4 Cl⁻ (bottom, purple solution).

In addition to UV-Visible titration, the host-guest complexation between P(DMAEMA-*co*-NaphtA) and CBPQT⁴⁺, 4 Cl⁻ was investigated by ¹H NMR spectroscopy in D₂O (**Figure S4** and **Figure 3**). The comparison of the ¹H NMR spectrum of the complexed copolymer (**Figure 3B**) with the spectrum of the non-complexed copolymer (**Figure 3A**) and CBPQT⁴⁺, 4 Cl⁻ (**Figure 3C**) showed the expected characteristic chemical shifts both of H_α, H_β, and H_{ph} signals from CBPQT⁴⁺, 4 Cl⁻ and of H_{2/6}, H_{3/7} and H_{4/8} from the naphthalene units, thereby providing further evidence for complete complexation of the naphthalene units after the addition of 5 equivalents of CBPQT⁴⁺, 4 Cl⁻. In addition, below the equivalence point, it is noteworthy that

the signals of the protons corresponding to both the non-complexed and complexed naphthalene moieties are clearly visible, indicating a slow exchange on the NMR timescale (≈ 10 ms) between the free and complexed assemblies (**Figure S4**).

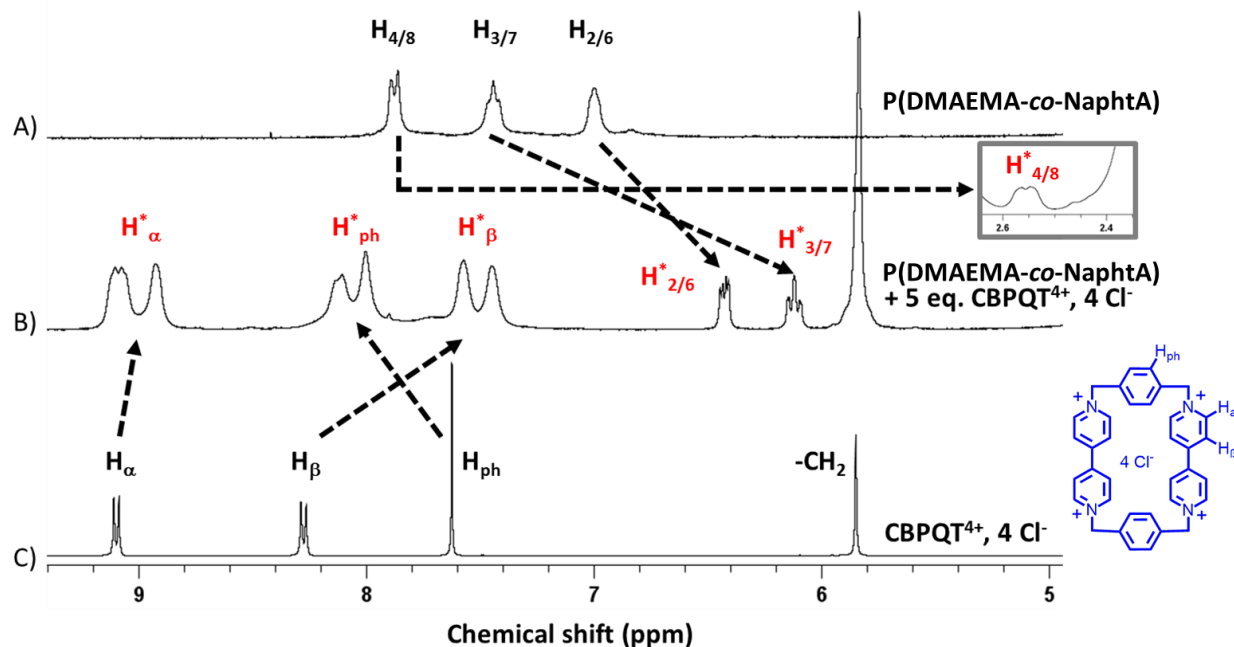


Figure 3. Partial ^1H NMR (D_2O) spectra of A) $\text{P(DMAEMA-co-NaphtA)}$ copolymer, B) $\text{P(DMAEMA-co-NaphtA)}$ copolymer with 5 eq. of CBPQT^{4+} , 4Cl^- and C) CBPQT^{4+} , 4Cl^- alone. The protons H^* denote complexed protons from naphthalene units and CBPQT^{4+} , 4Cl^- .

Host-guest binding of $\text{P(DMAEMA-co-NaphtA)}$ copolymer with CBPQT^{4+} , 4Cl^- was also investigated by isothermal titration microcalorimetry (ITC). The ITC experiments (**Figure S5**) showed that addition of CBPQT^{4+} , 4Cl^- to a dilute aqueous solution of $\text{P(DMAEMA-co-NaphtA)}$ copolymer at 20°C gives rise to a high association constant $K_a = 6.5 \times 10^5 \text{ M}^{-1}$, an exothermic response with $\Delta H = -68.5 \text{ kJ}\cdot\text{mol}^{-1}$ and $\Delta S = -0.12 \text{ kJ}\cdot\text{mol}^{-1}$, and a stoichiometry of 3.90). The K_a value obtained by ITC is in agreement with the value calculated from the UV-Visible titration.

Responsiveness of P(DMAEMA-co-NaphtA) copolymer in water solution. As mentioned in the introduction, the PDMAEMA homopolymer shows a pH-dependent LCST behavior with a pK_a around 7.0-7.5.²⁹⁻³¹ The pK_a value for the P(DMAEMA-co-NaphtA) copolymer in aqueous solution was 7.25, as determined by potentiometry titration (**Figure S6**). Since a pH increase leads to an increase in the protonation degree of the tertiary amine groups and to a drastic increase of the T_{CP} values or even to the loss of the thermo-responsive properties, the thermoresponsiveness was evaluated by UV-Visible spectroscopy at different pH values, (*i.e.* 8.5, 9 and 9.5), compatible with a clear reading of the T_{CP} value and keeping in mind that CBPQT⁴⁺, 4 Cl⁻ starts degrading at pH values higher than 9.5. The degree of ionization (α) of the tertiary amine units as a function of pH was calculated from the potentiometry titration curve (**Figure S6**). At pH 9.5, 9 and 8, the α values were 0, 0.02 and 0.06 respectively. The non-complexed P(DMAEMA-co-NaphtA) freshly prepared solution in deionized water exhibited a pH value of 9.5 ($\alpha = 0$) and showed a sharp phase transition with a T_{CP} of 30 °C, which is lower than for the PDMAEMA homopolymer that was reported to exhibit a T_{CP} of 46.6 °C.²⁵ This result is consistent with the more hydrophobic character resulting from the incorporation of the naphthalene-based units in the copolymer. We next investigated the impact of the host-guest complexation on the T_{CP} of the copolymer through the successive addition of CBPQT⁴⁺, 4 Cl⁻ (**Figure 4A**). Interestingly, at pH 9.5, a linear increase of the T_{CP} values was observed from 30 °C for 0 eq. to 38 °C for 5 eq. of CBPQT⁴⁺, 4 Cl⁻ (**Figure 4B**). This behavior can be explained by the complexation of the naphthalene units with the more hydrophilic CBPQT⁴⁺, 4 Cl⁻ host, which masks the hydrophobic naphthalene groups upon host-guest complexation. This results also showed that each successively formed complex has a strong, rather similar, effect on the overall hydrophilicity of copolymer. Conversely, the T_{CP} of a solution containing the copolymer with an unknown amount of CBPQT⁴⁺, 4 Cl⁻, would directly

indicate the number of host-guest complexes and the polymer may, thus, be further developed for sensing of unknown CBPQT^{4+} , 4 Cl^- concentrations.

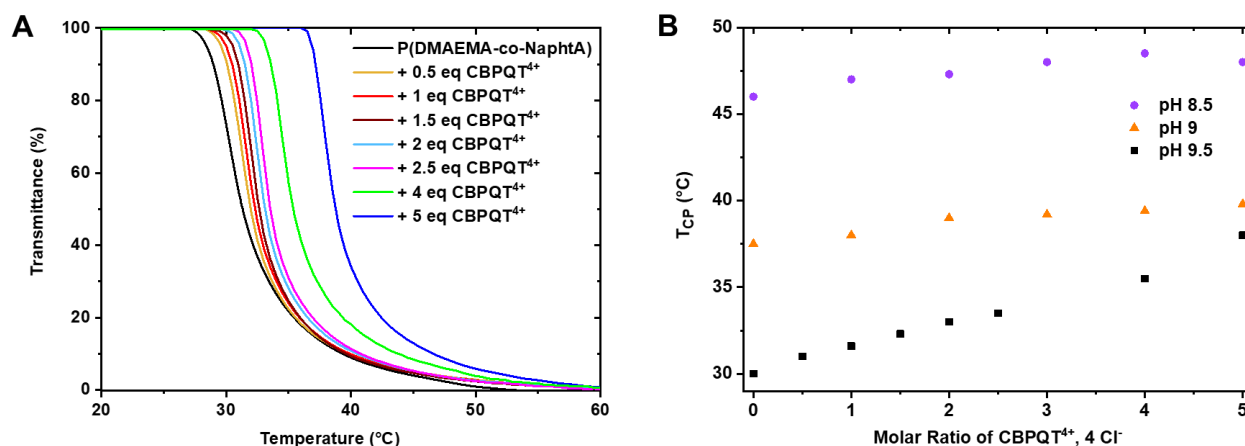


Figure 4. A) Turbidimetry of P(DMAEMA-*co*-NaphtA) copolymer solutions complexed with CBPQT^{4+} , 4 Cl^- (from 0 to 5 equivalents) as measured by UV-Visible spectroscopy at 800 nm with a polymer concentration of 5 g.L^{-1} at pH 9.5. B) Dependence of T_{CP} of P(DMAEMA-*co*-NaphtA) copolymer *versus* molar ratio of CBPQT^{4+} , 4 Cl^- added, at different pH values.

In order to adjust the pH of the solutions to pH 9 ($\alpha = 0.02$) and 8.5 ($\alpha = 0.06$), freshly prepared solutions of P(DMAEMA-*co*-NaphtA) were subjected to CO_2 bubbling. The pH decrease was accompanied by an increase in hydrophilicity of the copolymer resulting from partial protonation of the tertiary amine moieties and consequently led to an increase in the T_{CP} values, to $37.5 \text{ }^\circ\text{C}$ for pH 9 and $46 \text{ }^\circ\text{C}$ for pH 8.5 (**Figure S7** and **Figure 4B**). Successive additions of CBPQT^{4+} , 4 Cl^- induced a slight linear increase of about $2 \text{ }^\circ\text{C}$ on the T_{CP} values (from $37.5 \text{ }^\circ\text{C}$ to $39.8 \text{ }^\circ\text{C}$ and from $46 \text{ }^\circ\text{C}$ to $48 \text{ }^\circ\text{C}$ for pH 9 and 8.5 respectively), showing that the formation of the host-guest complexes had a weaker effect on the overall hydrophilicity of the copolymer at lower pH than at pH 9.5. At these lower pH values, the influence of the host-guest complexation with the charged CBPQT^{4+} , 4 Cl^- on the overall polymer hydrophilicity is

apparently diminished due to presence of the positive charges on the polymer itself. The behavior of the copolymer is more driven by the degree of ionization, for $\alpha > 0$, than by the complexation. This study, thus, highlights the ability to finely tune the T_{CP} of the copolymer solution over a large temperature window (from 30 °C to 48 °C), by adjusting the number of $CBPQT^{4+}$, 4 Cl^- equivalents and the pH. Moreover, the supramolecular assemblies between the $P(DMAEMA-co-NaphtA)$ copolymer and $CBPQT^{4+}$, 4 Cl^- act as programmable thermometers thanks to their linear response and an associated colored readout.

During the studies on the thermoresponsive behavior of $P(DMAEMA-co-NaphtA)$ complexed with $CBPQT^{4+}$, 4 Cl^- at pH 9.5, it was visually noticed that the turbid solution and the pellet of the collapsed polymer, that was isolated from the solution by centrifugation, at 60 °C ($T > T_{CP}$) remained colored, meaning that the host-guest complexation was retained, at least partially, above the T_{CP} (**Figure 5**).

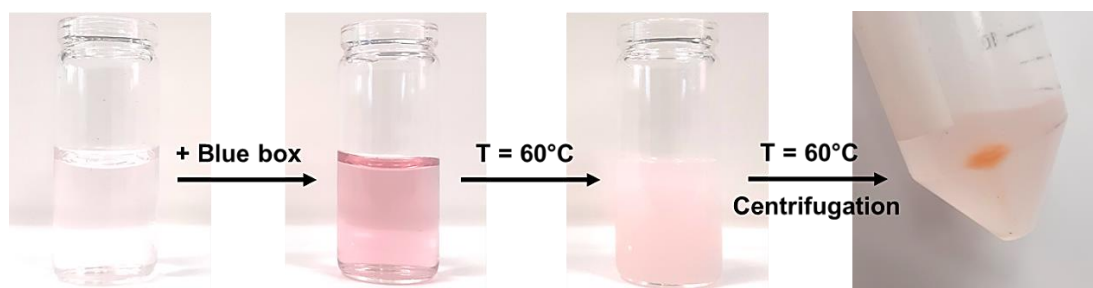


Figure 5. Pictures of a solution of $P(DMAEMA-co-NaphtA)$ copolymer (5 g.L⁻¹) with zero, five equivalents of $CBPQT^{4+}$, 4 Cl^- below the cloud point, five equivalents of $CBPQT^{4+}$, 4 Cl^- above the cloud point before centrifugation and above the cloud point after centrifugation (from left to right).

To further investigate this observation, variable temperature ¹H NMR spectroscopy of the complexed copolymer (*i.e.* with 5 equivalents of $CBPQT^{4+}$, 4 Cl^-) was performed at 20 °C (below T_{CP}) and at 70 °C (above T_{CP}). From **Figure 6**, it appears that the characteristic

resonance signals of the DMAEMA units drastically decreased in intensity (from 1 to 4 ppm) when the solution was heated above temperature its T_{CP} ($T = 70\text{ }^{\circ}\text{C}$), as expected for LCST-type (co)polymers due to partial dehydration of the polymer.³⁵

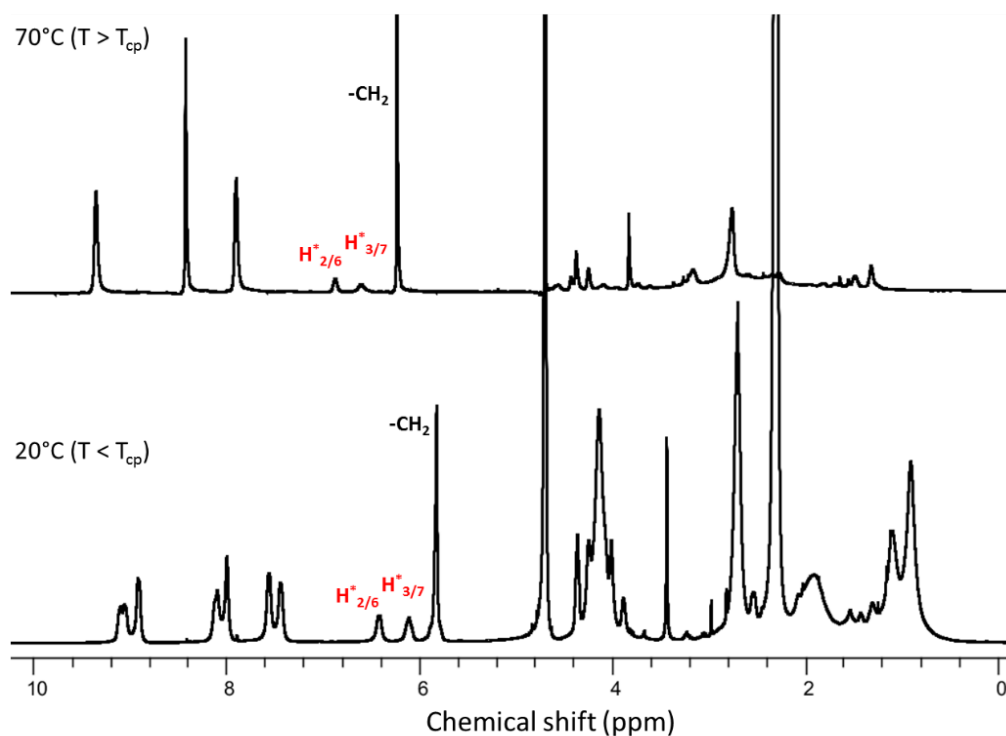


Figure 6. ^1H NMR spectra (D_2O) of P(DMAEMA-*co*-NaphtA) copolymer solution at pH 9.5 and with CBPQT^{4+} , 4 Cl^- at $20\text{ }^{\circ}\text{C}$ ($T < T_{CP}$) and at $70\text{ }^{\circ}\text{C}$ ($T > T_{CP}$). The protons H^* denote complexed protons from the naphthalene units while the $-\text{CH}_2$ belongs to both the free and complexed CBPQT^{4+} , 4 Cl^- host.

Nevertheless, both signals of $\text{H}^*_{3/7}$ and $\text{H}^*_{2/6}$ from the complexed naphthalene were still visible between 6 and 6.5 ppm (**Figure 6**), clearly showing that the host-guest complex is still present at $70\text{ }^{\circ}\text{C}$. In addition, although the signals corresponding to the DMAEMA subunits were clearly attenuated at $70\text{ }^{\circ}\text{C}$, they were still present at 2.8 ppm and between 1.2 and 1.6 ppm, as already observed in literature for PDMAEMA homopolymers³⁶ and copolymers³⁷. Furthermore, by comparing the integrals of the signals of the complexed $\text{H}^*_{3/7}$ and $\text{H}^*_{2/6}$ to the CH_2 protons of

CBPQT⁴⁺, 4 Cl⁻ at 5.8 ppm below and above the T_{CP} (**Figure S8**), it could be determined that approximately 52% of the complexes remained intact at 70 °C. From these results, it can be concluded that the polymer phase transition leads to the partial disruption of this host-guest complexation at pH 9.5. When decreasing the temperature below the T_{CP}, the host-guest complex was fully restored, meaning that the disassembly is fully reversible upon the temperature stimulus. This result is different compared to previously reported dialkoxynaphthalene end-functionalized polymers such as poly(*N*-isopropylacrylamide) (PNIPAm)²⁰ or poly(oligoethylene glycol acrylate)s,²² as well as naphthalene side-chain functionalized PNIPAm²¹ for which a complete dissociation was obtained when the temperature exceeded their T_{CP}, meaning that the microenvironment change of the polymer from the hydrophilic state to a collapsed hydrophobic state induced a complete host-guest complex disruption. This difference in behavior might be due to the fact that the PDMAEMA based polymers are less hydrophobic when exposed to temperature above the cloud point compared to PNIPAm. As a result, there will be more water remaining in the collapsed high polymer concentration phase and the hydrophobic driving force for host-guest complexation as well as hydration of the CBPQT⁴⁺, 4 Cl⁻ will be partially retained in the collapsed phase.

The decomplexation of the P(DMAEMA-*co*-NaphtA) copolymer with CBPQT⁴⁺, 4 Cl⁻ was also studied by UV-Visible spectroscopy upon the addition of sodium dodecyl sulfate (SDS). It has been previously reported that the anionic surfactant SDS triggers the anion exchange of dodecyl sulfate anions (DS⁻) with the chloride ion surrounding the cyclophane CBPQT⁴⁺, 4 Cl⁻ leading to the formation of CBPQT⁴⁺, 4 DS⁻, which is insoluble in aqueous media and inducing the decomplexation by precipitation of the host from water.³⁸ **Figure 7** shows the evolution of the absorbance at 520 nm corresponding to the charge transfer band upon the addition of CBPQT⁴⁺, 4 Cl⁻ to the P(DMAEMA-*co*-NaphtA) copolymer, which is subsequently followed by the progressive addition of SDS.

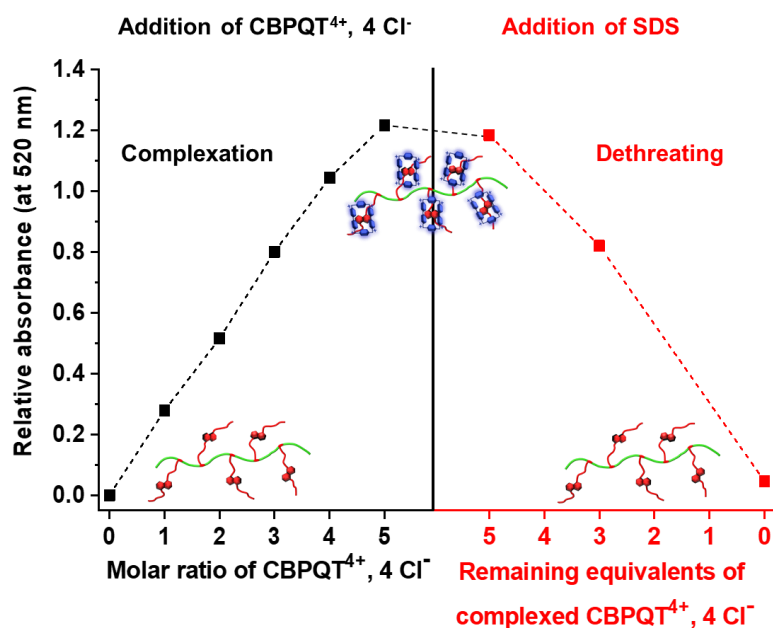


Figure 7. Evolution of the absorbance of the charge transfer band (centered at 520 nm) corresponding to the complexation between P(DMAEMA-*co*-NaphtA) copolymer (in deionized water, 5 g.L⁻¹) upon addition of equivalents CBPQT⁴⁺, 4 Cl⁻ (black squares, from 0 to 5 equivalents) followed by the addition of the anionic surfactant SDS (red squares).

As previously discussed, the absorbance of the charge transfer band, resulting from the host-guest complexation, linearly increased until the addition of 5 equivalents of CBPQT⁴⁺, 4 Cl⁻. To the solution containing the copolymer fully complexed with 5 equivalents of CBPQT⁴⁺, 4 Cl⁻, the SDS was added in a stepwise manner. When 2 equivalents of SDS (*i.e.* 8 SDS molecules for 2 CBPQT⁴⁺, 4 Cl⁻ units) were added, a similar absorbance value was obtained as the one obtained during the direct titration of the polymer complexed with 3 equivalents of CBPQT⁴⁺, 4 Cl⁻. This means that the 2 equivalents of SDS (*i.e.* towards CBPQT⁴⁺, 4 Cl⁻) added to the solution were utilized for the anion exchange of 2 equivalents of CBPQT⁴⁺, 4 Cl⁻ into CBPQT⁴⁺, 4 DS⁻. It is noteworthy that this counter-ion exchange was accompanied by the appearance of a precipitate in solution, which was carefully filtered for UV-Vis spectroscopy analysis, due to the water insolubility of the tetracationic cyclophane associated with four dodecyl sulfate anions

CBPQT⁴⁺,4 DS⁻.³⁸ Furthermore, the final addition of 3 equivalents of SDS (*i.e.* 12 SDS molecules for 3 CBPQT⁴⁺, 4 Cl⁻ units) to the solution resulted in a colorless solution (after careful filtration of the formed precipitate CBPQT⁴⁺, 4 DS⁻) and the absorbance recorded at a wavelength of 520 nm was close to 0, clearly demonstrating that no complex between CBPQT⁴⁺, 4 Cl⁻ and P(DMAEMA-*co*-NaphtA) copolymer was left in solution. This experiment clearly demonstrates the ability to finely tune the extent of (de)complexation and then the corresponding color intensity of the solution, by addition of the SDS surfactant to a supramolecular assembly of the CBPQT⁴⁺, 4 Cl⁻ host and the naphthalene functionalized copolymer. Moreover, this latter experiment demonstrates the additional benefit of separating, in an easy way, the uncomplexed polymer and the tetracationic host.

Conclusions

In conclusion, we have shown that the naphthalene-based monomer (NaphtA) can be copolymerized with DMAEMA *by* RAFT polymerization to obtain a well-defined P(DMAEMA-*co*-NaphtA) copolymer. The absorbance of the charge transfer band in the visible region increased linearly during the addition of the host CBPQT⁴⁺, 4 Cl⁻ molecule, clearly demonstrating that the complexation rate and thus, the color intensity of the solution, can be programmed with a direct visual read-out. Moreover, turbidity measurements of the thermoresponsive P(DMAEMA-*co*-NaphtA) copolymer bearing electron-rich pendant naphthalene guest units revealed that its T_{CP} could be adjusted between 30 °C and 48 °C by the number of CBPQT⁴⁺, 4 Cl⁻ equivalents added and the pH value. Interestingly, we have also demonstrated that, according to the applied stimulus, the response of the complexed copolymers is different, indicating that the host-guest complexation state can be controlled. By heating the host-guest polymer complex above the T_{CP}, a partial dethreading was observed while adding aliquots of the anionic surfactant SDS leads to the tunable disruption of the host-guest complex up to full decomplexation, thanks to the anion exchange of the four Cl⁻ counter-ions surrounding

the CBPQT⁴⁺ to four DS⁻ resulting in a hydrophobic CBPQT⁴⁺, 4 DS⁻ that precipitates from the aqueous solution.

Data availability statement

The raw/processed data required to reproduce these findings cannot be shared at this time due to technical or time limitations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version.

References

1. Lehn, J.-M., Towards complex matter: supramolecular chemistry and self-organization. *European Review* **2009**, *17* (2), 263-280.
2. Mattia, E.; Otto, S., Supramolecular systems chemistry. *Nature nanotechnology* **2015**, *10* (2), 111-119.
3. Gloe, K., *Macrocyclic chemistry*. Springer: 2005.
4. Vögtle, F.; Weber, E., *Host Guest Complex Chemistry Macrocycles: Synthesis, Structures, Applications*. Springer Science & Business Media: 2012.
5. Dong, S.; Zheng, B.; Wang, F.; Huang, F., Supramolecular polymers constructed from macrocycle-based host-guest molecular recognition motifs. *Accounts of chemical research* **2014**, *47* (7), 1982-1994.
6. Ji, X.; Ahmed, M.; Long, L.; Khashab, N. M.; Huang, F.; Sessler, J. L., Adhesive supramolecular polymeric materials constructed from macrocycle-based host-guest interactions. *Chemical Society Reviews* **2019**, *48* (10), 2682-2697.
7. Xiao, T.; Xu, L.; Zhou, L.; Sun, X.-Q.; Lin, C.; Wang, L., Dynamic hydrogels mediated by macrocyclic host-guest interactions. *Journal of Materials Chemistry B* **2019**, *7* (10), 1526-1540.
8. Blanco-Gómez, A.; Cortón, P.; Barravecchia, L.; Neira, I.; Pazos, E.; Peinador, C.; García, M. D., Controlled binding of organic guests by stimuli-responsive macrocycles. *Chemical Society Reviews* **2020**.
9. Ritter, H.; Sadowski, O.; Tepper, E., Influence of Cyclodextrin Molecules on the Synthesis and the Thermoresponsive Solution Behavior of N-Isopropylacrylamide Copolymers with Adamantyl Groups in the Side-Chains. *Angewandte Chemie International Edition* **2003**, *42* (27), 3171-3173.
10. 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. *Journal of the American Chemical Society* **2007**, *129* (12), 3502-3503.
11. Gingter, S.; Bezdushna, E.; Ritter, H., Chiral Recognition of Poly(N-isopropylacrylamide-co-(d or l)-N-tryptophan-acrylamide) with Methylated β -Cyclodextrin. *Macromolecules* **2010**, *43* (7), 3128-3131.
12. Schmidt, B. V. K. J.; Rudolph, T.; Hetzer, M.; Ritter, H.; Schacher, F. H.; Barner-Kowollik, C., Supramolecular three-armed star polymers via cyclodextrin host-guest self-assembly. *Polymer Chemistry* **2012**, *3* (11), 3139-3145.
13. Jia, Y.-G.; Zhu, X. X., Thermoresponsiveness of Copolymers Bearing Cholic Acid Pendants Induced by Complexation with β -Cyclodextrin. *Langmuir* **2014**, *30* (39), 11770-11775.
14. de la Rosa, V. R.; Nau, W. M.; Hoogenboom, R., Tuning temperature responsive poly(2-alkyl-2-oxazoline)s by supramolecular host-guest interactions. *Organic & Biomolecular Chemistry* **2015**, *13* (10), 3048-3057.
15. de la Rosa, V. R.; Nau, M. W.; Hoogenboom, R., Thermoresponsive Interplay of Water Insoluble Poly(2-alkyl-2-oxazoline)s Composition and Supramolecular Host-Guest Interactions. *International Journal of Molecular Sciences* **2015**, *16* (4), 7428-7444.
16. Van Guyse, J. F. R.; Bera, D.; Hoogenboom, R., Adamantane Functionalized Poly(2-oxazoline)s with Broadly Tunable LCST-Behavior by Molecular Recognition. *Polymers* **2021**, *13* (3), 374.
17. Rauwald, U.; Barrio, J. d.; Loh, X. J.; Scherman, O. A., "On-demand" control of thermoresponsive properties of poly(N-isopropylacrylamide) with cucurbit[8]uril host-guest

complexes. *Chemical Communications (Cambridge, United Kingdom)* **2011**, 47 (21), 6000-6002.

18. Ji, X.; Chen, J.; Chi, X.; Huang, F., pH-Responsive Supramolecular Control of Polymer Thermoresponsive Behavior by Pillararene-Based Host–Guest Interactions. *ACS Macro Letters* **2014**, 3 (1), 110-113.

19. Yu, G.; Zhou, J.; Chi, X., Pillar[10]arene-Based Size-Selective Host–Guest Complexation and Its Application in Tuning the LCST Behavior of a Thermoresponsive Polymer. *Macromolecular Rapid Communications* **2015**, 36 (1), 23-30.

20. Bigot, J.; Bria, M.; Caldwell, S. T.; Cazaux, F.; Cooper, A.; Charleux, B.; Cooke, G.; Fitzpatrick, B.; Fournier, D.; Lyskawa, J.; Nutley, M.; Stoffelbach, F.; Woisel, P., LCST: a powerful tool to control complexation between a dialkoxynaphthalene-functionalised poly(N-isopropylacrylamide) and CBPQT4+ in water. *Chemical Communications* **2009**, (35), 5266-5268.

21. Sambe, L.; de la Rosa, V. R.; Belal, K.; Stoffelbach, F.; Lyskawa, J.; Delattre, F.; Bria, M.; Cooke, G.; Hoogenboom, R.; Woisel, P., Programmable Polymer- Based Supramolecular Temperature Sensor with a Memory Function. *Angewandte Chemie International Edition* **2014**, 53 (20), 5044-5048.

22. Yeniad, B.; Ryskulova, K.; Fournier, D.; Lyskawa, J.; Cooke, G.; Woisel, P.; Hoogenboom, R., Complexation of thermoresponsive dialkoxynaphthalene end-functionalized poly(oligoethylene glycol acrylate)s with CBPQT4+ in water. *Polymer Chemistry* **2016**, 7 (22), 3681-3690.

23. Guo, H.; Hourdet, D.; Marcellan, A.; Stoffelbach, F.; Lyskawa, J.; De Smet, L.; Vebr, A.; Hoogenboom, R.; Woisel, P., Dual Responsive Regulation of Host–Guest Complexation in Aqueous Media to Control Partial Release of the Host. *Chemistry–A European Journal* **2020**, 26 (6), 1292-1297.

24. Bütünb, V.; Armes, S. P.; Billingham, N. C., Synthesis and aqueous solution properties of near-monodisperse tertiary amine methacrylate homopolymers and diblock copolymers. *Polymer* **2001**, 42 (14), 5993-6008.

25. Fournier, D.; Hoogenboom, R.; Thijs, H. M. L.; Paulus, R. M.; Schubert, U. S., Tunable pH- and Temperature-Sensitive Copolymer Libraries by Reversible Addition-Fragmentation Chain Transfer Copolymerizations of Methacrylates. *Macromolecules* **2007**, 40 (4), 915-920.

26. Plamper, F. A.; Ballauff, M.; Müller, A. H. E., Tuning the Thermoresponsiveness of Weak Polyelectrolytes by pH and Light: Lower and Upper Critical-Solution Temperature of Poly(N,N-dimethylaminoethyl methacrylate). *Journal of the American Chemical Society* **2007**, 129 (47), 14538-14539.

27. Dong, Z.; Wei, H.; Mao, J.; Wang, D.; Yang, M.; Bo, S.; Ji, X., Synthesis and responsive behavior of poly(N,N-dimethylaminoethyl methacrylate) brushes grafted on silica nanoparticles and their quaternized derivatives. *Polymer* **2012**, 53 (10), 2074-2084.

28. Cao, Y.; Liu, N.; Fu, C.; Li, K.; Tao, L.; Feng, L.; Wei, Y., Thermo and pH Dual-Responsive Materials for Controllable Oil/Water Separation. *ACS Applied Materials & Interfaces* **2014**, 6 (3), 2026-2030.

29. Yañez-Macias, R.; Alvarez-Moises, I.; Perevyazko, I.; Lezov, A.; Guerrero-Santos, R.; Schubert, U. S.; Guerrero-Sanchez, C., Effect of the Degree of Quaternization and Molar Mass on the Cloud Point of Poly[2-(dimethylamino)ethyl methacrylate] Aqueous Solutions: A Systematic Investigation. *Macromolecular Chemistry and Physics* **2017**, 218 (10), 1700065.

30. Xu, F.-J.; Kang, E.-T.; Neoh, K.-G., pH-and temperature-responsive hydrogels from crosslinked triblock copolymers prepared via consecutive atom transfer radical polymerizations. *Biomaterials* **2006**, 27 (14), 2787-2797.

31. Ding, A.; Lu, G.; Guo, H.; Huang, X., PDMAEMA-b-PPOA-b-PDMAEMA double-bond-containing amphiphilic triblock copolymer: synthesis, characterization, and pH-responsive self-assembly. *Polymer Chemistry* **2017**, *8* (43), 6628-6635.
32. Asakawa, M.; Dehaen, W.; L'Abbe, G.; Menzer, S.; Nouwen, J.; Raymo, F. M.; Stoddart, J. F.; Williams, D. J., Improved Template-Directed Synthesis of Cyclobis(paraquat-p-phenylene). *Journal of Organic Chemistry* **1996**, *61* (26), 9591-9595.
33. Connors, K. A., *Binding constants: the measurement of molecular complex stability*. Wiley-Interscience: 1987.
34. Hargrove, A. E.; Zhong, Z.; Sessler, J. L.; Anslyn, E. V., Algorithms for the determination of binding constants and enantiomeric excess in complex host: guest equilibria using optical measurements. *New Journal of Chemistry* **2010**, *34* (2), 348-354.
35. Zhang, Q.; Weber, C.; Schubert, U. S.; Hoogenboom, R., Thermoresponsive polymers with lower critical solution temperature: from fundamental aspects and measuring techniques to recommended turbidimetry conditions. *Materials Horizons* **2017**, *4* (2), 109-116.
36. Li, W.; Gao, C.; Qian, H.; Ren, J.; Yan, D., Multiamino-functionalized carbon nanotubes and their applications in loading quantum dots and magnetic nanoparticles. *Journal of Materials Chemistry* **2006**, *16* (19), 1852-1859.
37. Pietsch, C.; Mansfeld, U.; Guerrero-Sanchez, C.; Hoepfner, S.; Vollrath, A.; Wagner, M.; Hoogenboom, R.; Saubern, S.; Thang, S. H.; Becer, C. R.; Chiefari, J.; Schubert, U. S., Thermo-Induced Self-Assembly of Responsive Poly(DMAEMA-b-DEGMA) Block Copolymers into Multi- and Unilamellar Vesicles. *Macromolecules* **2012**, *45* (23), 9292-9302.
38. Louisy, J.; Delattre, F.; Lyskawa, J.; Malfait, A.; Maclean, C. E.; Sambe, L.; Zhu, N.; Cooke, G.; Woisel, P., Surfactant-mediated control of CBPQT(4+)-dialkoxynaphthalene complexation. *Chemical Communications* **2011**, *47* (24), 6819-6821.

SUPPORTING INFORMATIONS

Supramolecular control over pH- and temperature-responsive dialkoxynaphthalene-functionalized poly(2-(dimethylamino)ethyl methacrylate) in water

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Synthesis of the NaphtA monomer. 4-(Dimethylamino)pyridine (DMAP, 0.1 eq., 0.286 mmol) and dicyclohexylcarbodiimide (DCC, 1.2 eq., 3.43 mmol) were added, at 0 °C and under a nitrogen atmosphere, to a solution of (1-[2-(2-hydroxyethoxy)ethoxy]-5-[2-(2-methoxyethoxy)ethoxy]naphthalene (1 g, 1 eq., 2.86 mmol) and acrylic acid (1.2 eq., 3.43 mmol) in dichloromethane (50 mL). The solution was stirred for 2 h at 0 °C and then at room temperature for 24 h. The DCU was filtered off and the solvent was removed in vacuo. The resulting oil was subjected to silica gel column flash chromatography (acetone/petroleum spirit: 3/7). Yield: 43%.

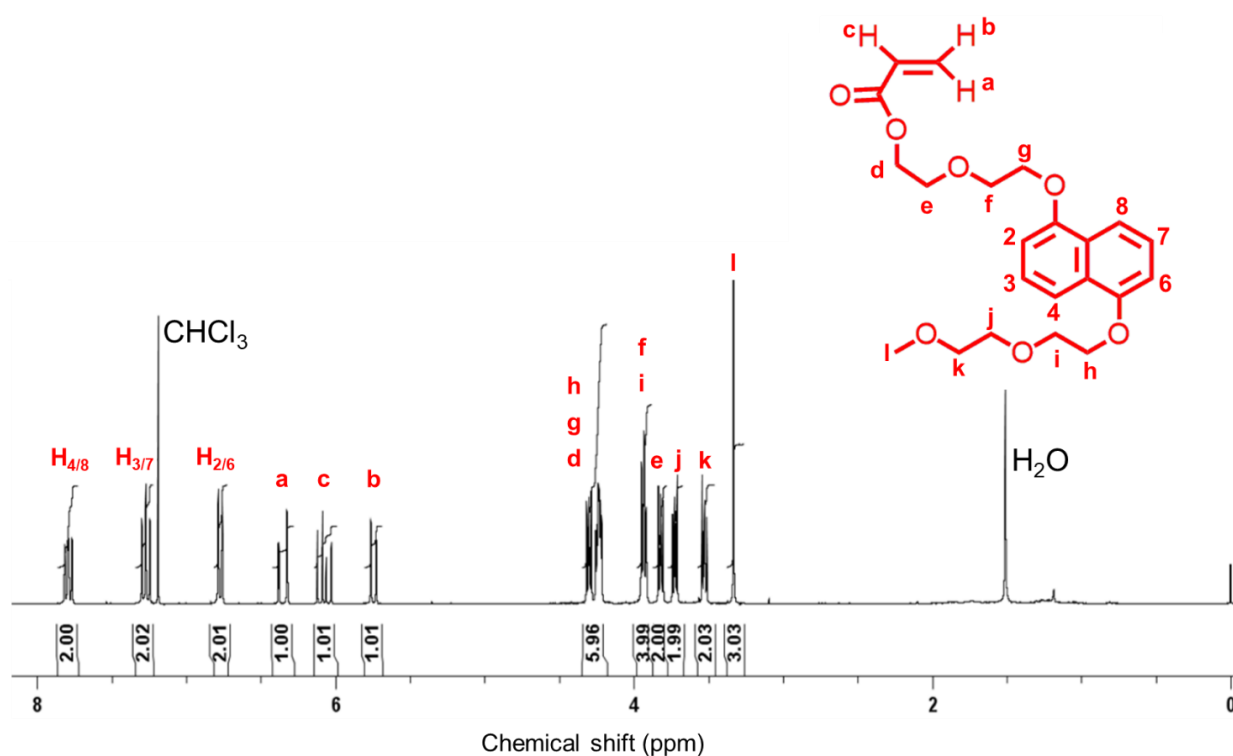


Figure S1. ^1H NMR spectrum (CDCl_3) of the NaphtA monomer.

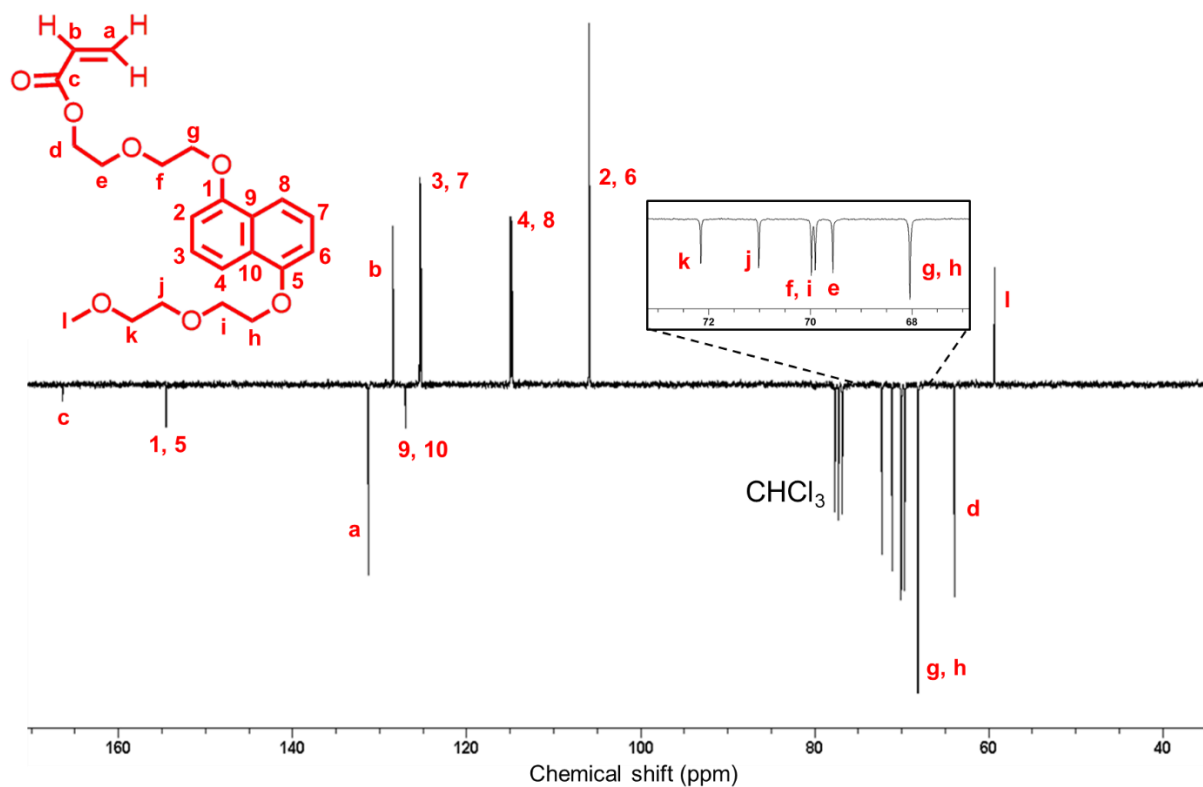


Figure S2. ^{13}C NMR spectrum (CDCl_3) of the NaphtA monomer.

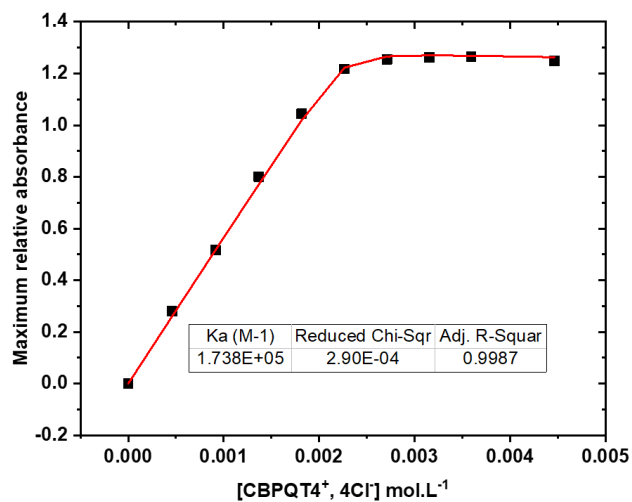


Figure S3. Determination of the association constant (K_a) by fitting the UV-Visible titration data using a non-linear regression. The fit curve is the red line and the fitting parameters obtained are summarized in the table.

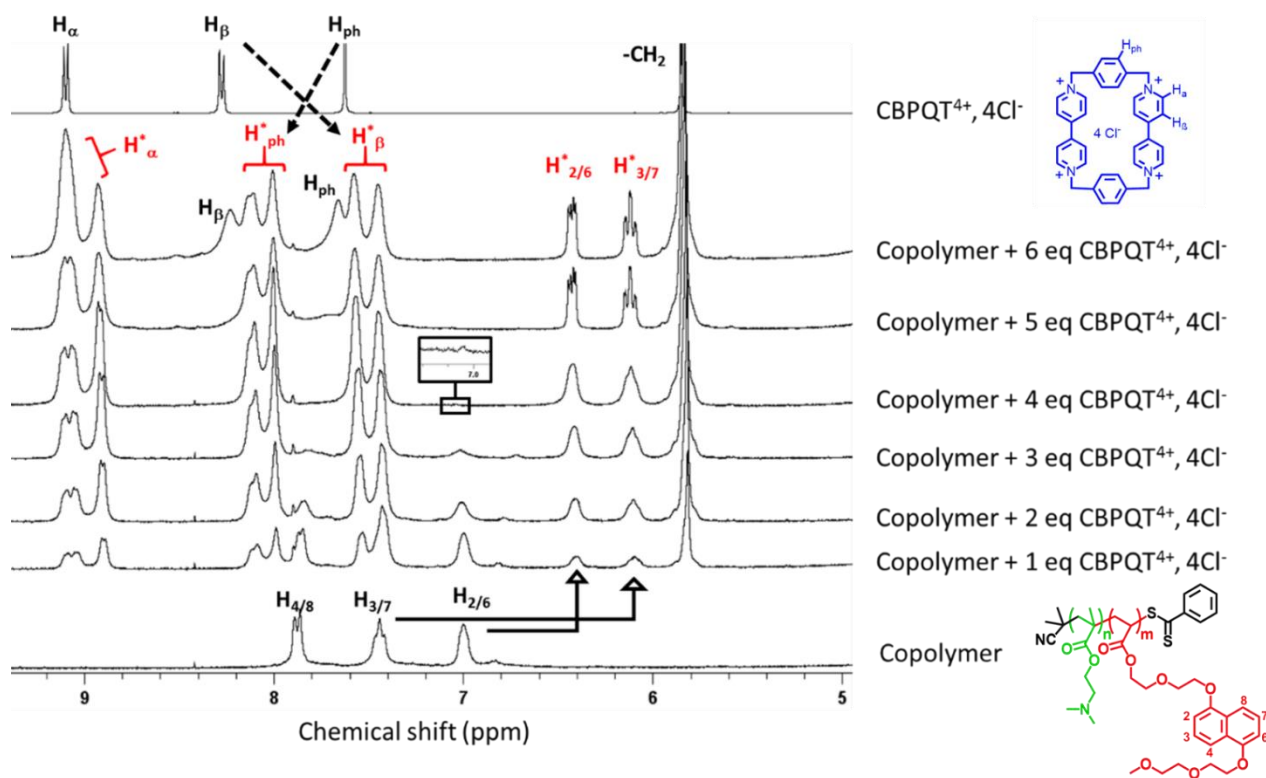


Figure S4. ^1H NMR titration (D_2O) of P(DMAEMA-*co*-NaphtA) copolymer upon addition of aliquots of CBPQT^{4+} , 4 Cl^- . The protons H^* denote complexed protons from naphthalene units and CBPQT^{4+} , 4 Cl^- .

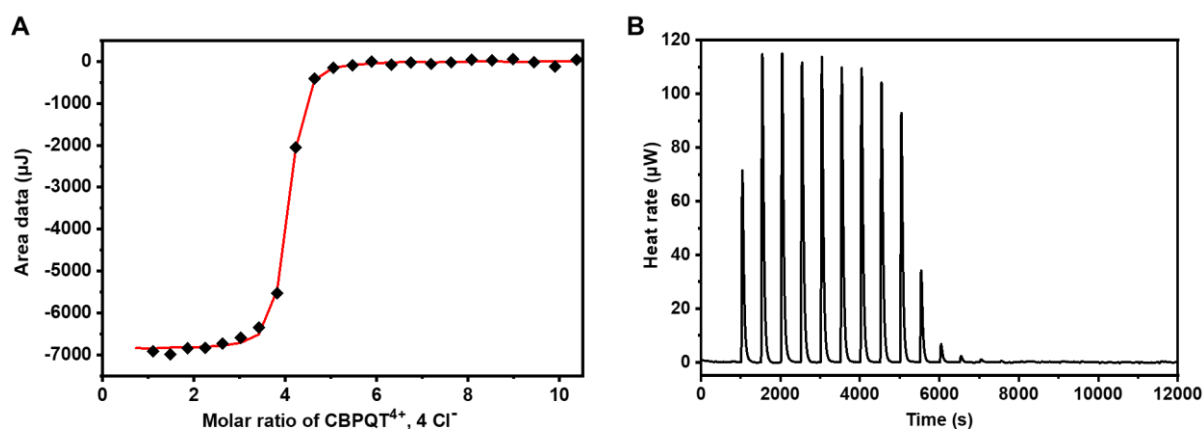


Figure S5. Isothermal titration calorimetry data for the addition of aliquots of CBPQT^{4+} , 4 Cl^- (10 mM) to P(DMAEMA-*co*-NaphtA) copolymer (0.292 mM). Recorded in H_2O at 20°C .

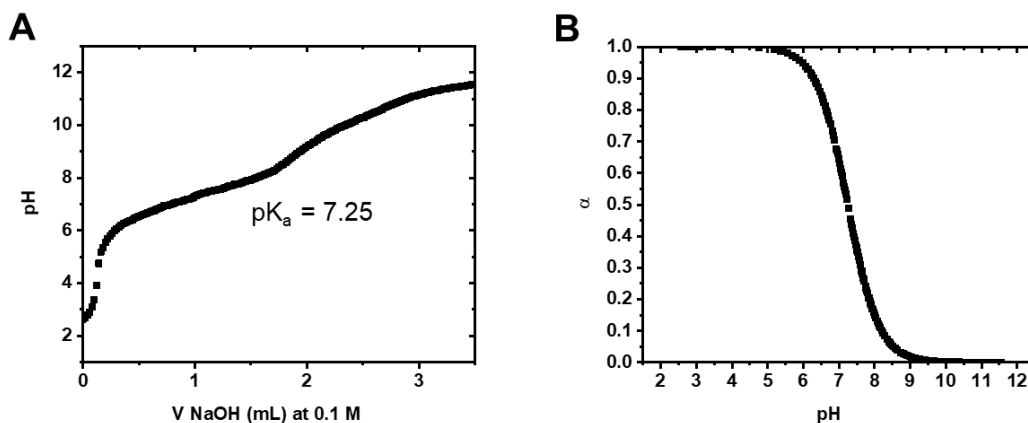


Figure S6. A) Evolution of the pH as a function of the added volume of 0.1 M NaOH and B) evaluation of the degree of ionization (α) with the pH for a solution of P(DMAEMA-*co*-NaphtA) copolymer at 5 g.mL⁻¹.

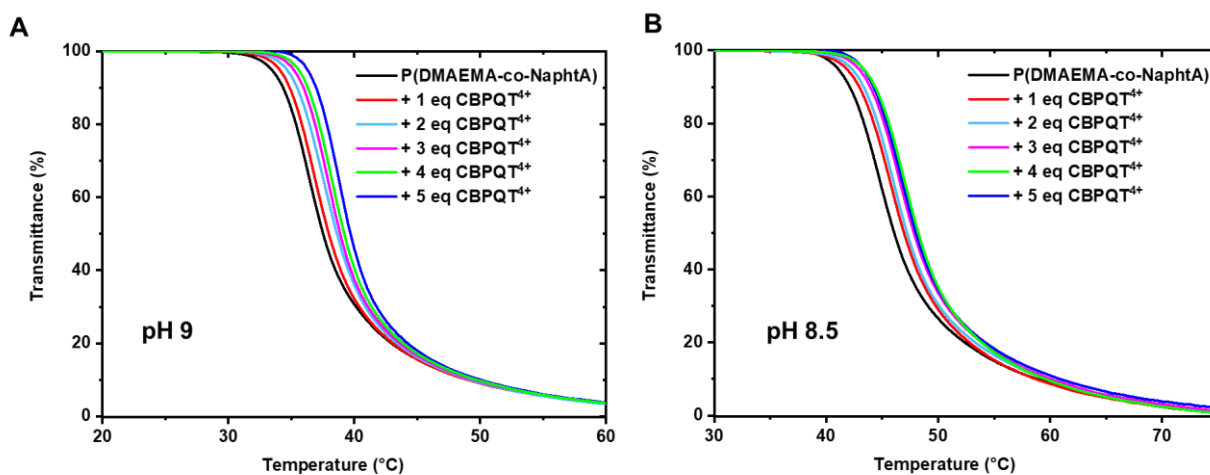


Figure S7. Phase transitions of P(DMAEMA-*co*-NaphtA) copolymer complexed with CBPQT⁴⁺, 4 Cl⁻ (from 0 to 5 equivalents) as measured by UV-Visible spectroscopy at 800 nm with a polymer concentration of 5 g.L⁻¹ at pH 9 (A) and pH 8.5 (B).

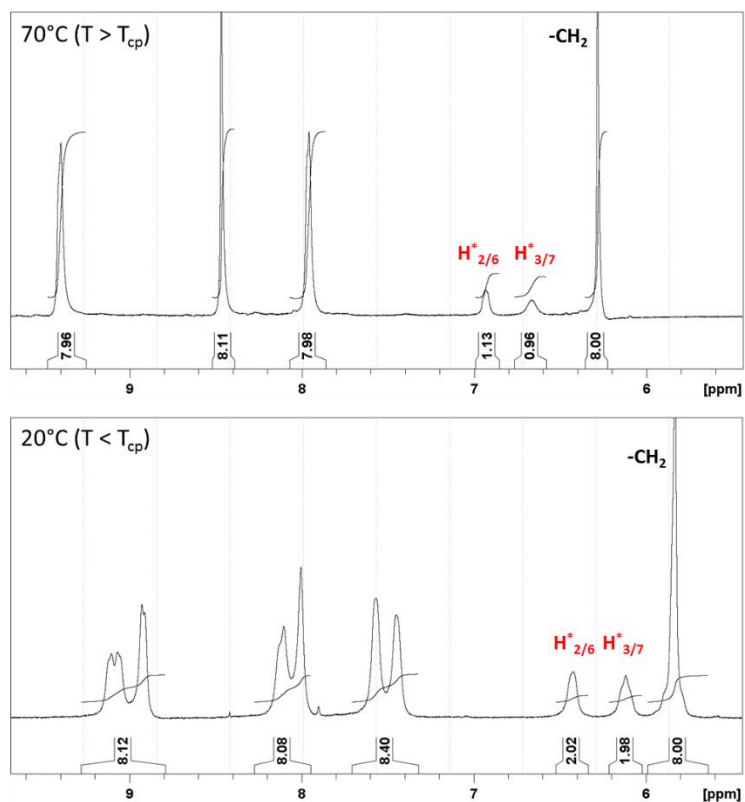


Figure S8. Partial ^1H NMR spectra (D₂O) of complexed P(DMAEMA-co-NaphtA) copolymer with CBPQT⁴⁺, 4 Cl⁻ (5 equivalents) at 20 °C ($T < T_{\text{CP}}$) and 70 °C ($T > T_{\text{CP}}$). The protons H* denote complexed protons from naphthalene units.