Fluorescent sensing of transition metal ions based on the encapsulation of dithranol in a polymeric core shell architecture†

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Received (in Cambridge, UK) 18th April 2005, Accepted 14th July 2005
First published as an Advance Article on the web 19th August 2005
DOI: 10.1039/b505409e

The encapsulation behaviour and the resulting transition metal ion sensing capabilities of a 5-arm star-shaped polymer bearing terpyridine ligands on its periphery are described.

The encapsulation of functionalities into polymeric or dendritic core shell architectures is a highly promising field of research due to the manifold application possibilities in drug delivery,[1,2] stimuli responsive release,[3] catalysis,[4,5] or phase transfer.[6–8] On the other hand, Patroni *et al.* recently described that a lipophilized ion receptor, a surfactant, and a fluorescent hydrocarbon (pyrene), are capable of forming micelles in water with the fluorophore included in them, that respond to Cu^{2+} and Ni^{2+} ions as selective fluorescent sensors.[9] We recently reported on the encapsulation and phase transfer behaviour of star-shaped block copolymers based on a poly(ethylene glycol) core and a poly(ε-caprolactone) corona.[10] Combining these two concepts we report here on the synthesis, encapsulation behaviour as well as the sensing application of a terpyridine end-group modified 5-arm star-shaped poly(ethylene glycol) polymer.

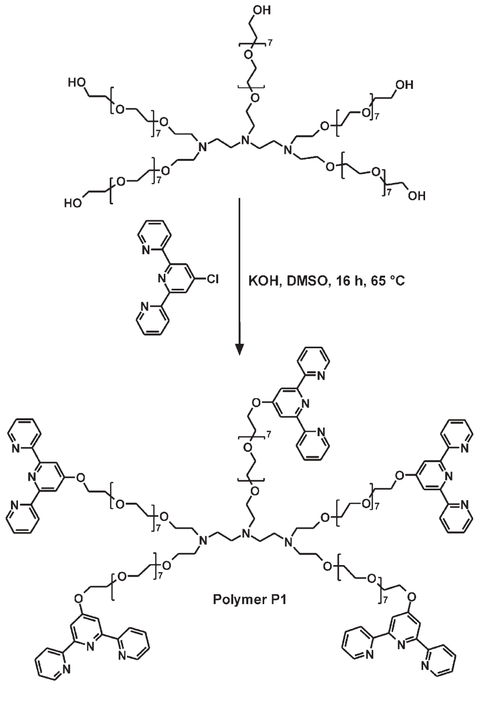

Fig. 1 Preparation and structure of the investigated polymer P1.

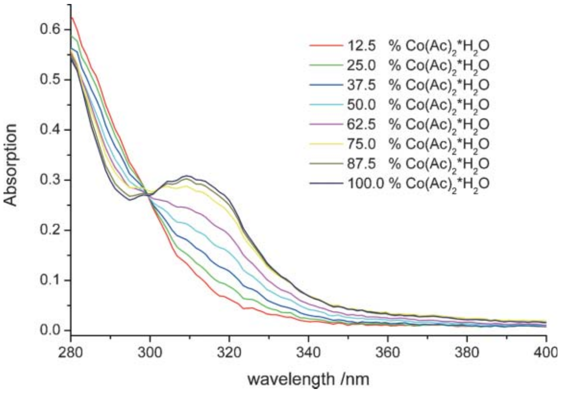

Fig. 2 Complexation behaviour of **P1** with a variety of transition metal ions investigated in a parallel fashion in DMSO. The displayed spectra detail the case of Co^{2+} ions.

Tridendate ligands, such as terpyridine (tpy), are known to form complexes with a large variety of transition metal ions[11] with high binding constants.[12] Moreover, these binding moieties are versatile building blocks in supramolecular and macromolecular chemistry,[13,14] leading to interesting materials such as supramolecular block copolymers[15] and their self assembled micelles[16,17] or multi-responsive polyelectrolyte gels.[18] Therefore, we utilized tpy ligands for the end-group modification of a 5-arm star-shaped poly(ethylene glycol) (PEG) polymer. The synthetic strategy as well as the structure of the resulting polymer are depicted in Fig. 1. All synthetic details, ^{1}H NMR, GPC as well as MALDI-TOFMS characterization data of polymer **P1** are provided in the supplementary information to this communication.†

Terpyridine ligands are capable of forming tpy-M^{2+}-tpy complexes with a variety of transition metal ions. To investigate this behaviour with polymer **P1**, a parallel titration experiment was performed with Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+} as well as Zn^{2+} salts in a microtiter plate. The layout of the microtiter plate is provided in the supplementary information.† The experiment clearly revealed that **P1**, but not the 5-arm PEG can form transition metal complexes with all investigated transition metal ions.

Moreover, Fig. 2 shows the resulting UV/Vis spectra of this experiment for the case of Co^{2+} ions. The increase of the π–π* band at 310 nm upon addition of Co^{2+} ions indicates the complex formation. A similar behaviour was found for the other investigated metal ions with π–π* bands in the region between

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† Electronic supplementary information (ESI) available: Experimental details, characterization data of **P1** as well as MALDI-TOFMS spectrum of **P1**. See http://dx.doi.org/10.1039/b505409e

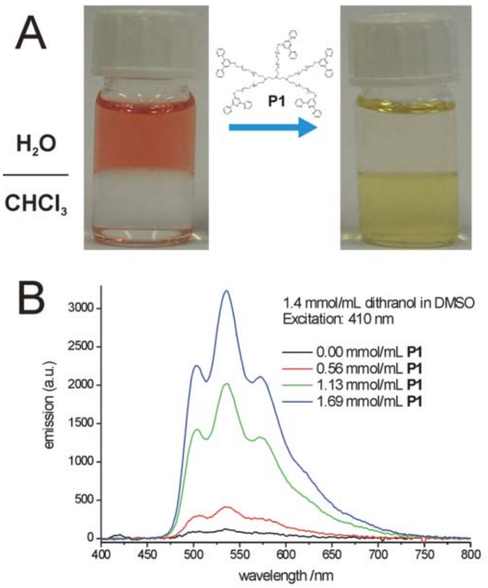


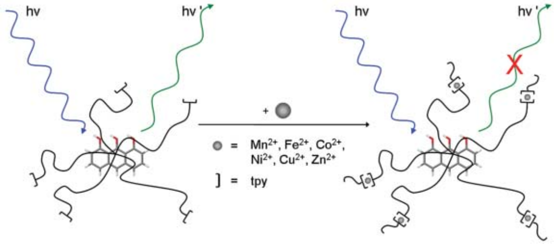
Fig. 3 Encapsulation behaviour of polymer **P1**. A: Encapsulation and phase transfer of methyl orange; B: encapsulation of dithranol measured by fluorescence spectroscopy. Chemical structures of the investigated guest molecules can be found in the supplementary information.†

300 and 330 nm. Moreover, the titration experiment revealed the typical metal-to-ligand-charge-transfer (MCLT) band at 556 nm for the tpy-Fe^{2+}-tpy complex. The formation of these transition metal complexes with **P1** leads to the formation of a supramolecularly cross-linked network. However, no undesired effects such as precipitation were observed in the investigated concentration ranges.

Polymer **P1** was also investigated regarding its encapsulation behaviour. In general, the encapsulation of a guest molecule within a host can be probed by the evaluation of changes in the guests microenvironment, which can be detected by spectroscopic techniques.[19] These changes are premised on stabilizing or destabilizing effects of the local microenvironment on electronic states of the guest molecules. Studies of **P1** in that regard revealed that it can encapsulate methyl orange, a pH indicator dye, in the same fashion as recently described for star-shaped block copolymers based on a poly(ethylene glycol) core and a poly(ε-caprolactone) corona.[10] Fig. 3A shows this encapsulation behaviour of methyl orange in polymer **P1** in a two phase (water/chloroform) system in a macroscopic fashion. The hydrophilic pH indicator dye is dissolved in the water phase, whereas upon addition of **P1** to the system the dye is encapsulated in the polymer and phase transferred since the polymer is more soluble in the chloroform phase than in the water phase. This encapsulation is accompanied by a colour change of methyl orange from red (λ_{max} = 504 nm) to yellow (λ_{max} = 420 nm) indicating a change in the microenvironment of the dye. It was already discussed recently that a hydrophobic barrier is necessary to obtain this encapsulation behaviour for the same starting 5-arm PEG polymer, but that the size of the hydrophobic barrier did not show any influence on the encapsulation behaviour of star-shaped block copolymers.[10] Therefore, the observed behaviour of **P1** suggests that the terpyridine ligands represent a sufficient hydrophobic barrier to obtain the described encapsulation and phase transfer behaviour. Moreover, it was observed that **P1** can encapsulate anthracene derivatives (such as dithranol or 9-hydroxymethylanthracene) from DMSO or chloroform solutions as it was also described in the literature for the corresponding star-shaped block copolymers.[20] Fig. 3B shows the encapsulation of dithranol within **P1** and the resulting increase of the fluorescence of the guest molecule depending on the concentration of added polymer. It was observed that dithranol : **P1** ratios higher than 1 : 1 lead to a decrease in the fluorescence of the guest, probably due to self-quenching effects. Therefore, a dithranol : **P1** ratio of 1 : 1 was chosen for all further experiments, since this ratio provided the highest fluorescence intensities.

The combination of the two described concepts of guest encapsulation and transition metal binding possibilities of polymer **P1** were subsequently investigated in a microtiter plate format utilizing a combined UV/Vis and Fluorescence reader. These studies revealed that the fluorescence intensity of encapsulated dithranol is decreasing upon addition of transition metal salts to the host–guest complex of dithranol and **P1**. This fluorescence quenching effect was observed for the binding of all investigated transition metal ions (Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}) and is depicted in Scheme 1. DMSO was used for these studies due to the good solubility of all components in this solvent. Dithranol was selected for these experiments, since its excitation wavelength of 410 nm does not overlap with any absorption bands of the investigated terpyridine metal complexes.

As described in the literature[9] and already mentioned above similar effects have been utilized for the sensoric detection of transition metal ions utilizing self assembled micelles. Fluorescent sensors are widely applied in different fields of research, such as the detection and quantification of proteins,[21] pH measurements[22] as well as for anion and cation quantification.[23] Generally, the cation and anion sensors are based on a covalent linkage of a fluorophore and a receptor site. Our approach utilized the self organization and encapsulation of a fluorophore within a polymer and requires only one synthetic step to functionalize the polymer with a receptor molecule. This approach has similar advantages as described for self-assembled micelles from lipophilized receptors, a sufactant and a fluorophore,[9] *e.g.* the choice of the fluorophore without synthetic effort as well as the variation of the receptor in only one synthetic step. However, our system cannot be used in water due to the low solubility of **P1** in water. Nevertheless, a significant advantage is the avoidance of the dynamic equilibrium between the individual small amphiphiles and the self-assembled micellar structure, which



Scheme 1 Fluorescence quenching behaviour of the dithranol–**P1** host guest complexes depending on the binding of transition metal ions (and therefore supramolecular network formation) to the terpyridine ligands.

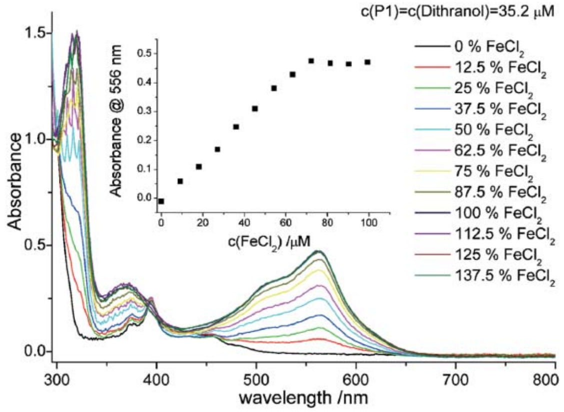


Fig. 4 UV/Vis response of the investigated sensoric system to Fe^{+2} ions.

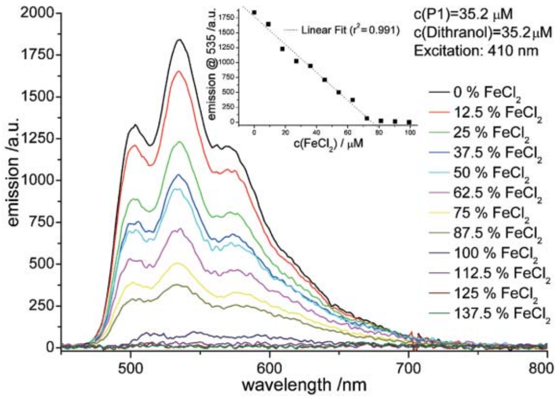


Fig. 5 Fluorescence response of the investigated sensoric system to Fe^{+2} ions.

might lead to undesired effects depending on temperature or ionic strength.

Figs. 4 and 5 display the response of the described sensor system to $FeCl_2$ in DMSO. Fig. 4 depicts the UV/Vis spectral changes upon addition of Fe^{2+} ions to the sensoric system. As expected the MLCT band at 556 nm is increasing until full *bis*-complexation of all terpyridine ligands is reached. The inset in Fig. 4 clearly reveals an equivalence point at 100% complexation. Fig. 5 shows the corresponding fluorescence signal of dithranol. The intensity is quenched upon addition of the transition metal salt until no detectable signal is observed (corresponding to full complexation of the ligands). This decrease in the fluorescence intensity of the encapsulated dithranol was not only observed for Fe^{2+} ions but for all investigated transition metal ions (Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}). The inset in Fig. 5 shows the decrease of the fluorescence intensity at its maximum at 535 nm. A linear correlation between this intensity and the concentration of transition metal ion was observed. Moreover, the dynamic range of this sensoric system was found to be in the micro-molar range of analyte. Therefore, the described sensor is not selective to a specific species but might be useful for the quantitation of the overall content of the mentioned transition metal ions. However, the linear response in the micro-molar range makes this system quite sensitive and detection of small quantities of the mentioned species is feasible.

In conclusion, we synthesized and evaluated a new material based on a 5-arm star-shaped poly(ethylene glycol), which was functionalized with terpyridine binding units. This material is capable of forming metal complexes with a variety of transion metal ions. Moreover, it was observed that the mentioned polymer allowed encapsulation of functional molecules, such as fluorescent anthracene derivatives. The combination of the two concepts lead to a new fluorescent sensor system for transition metal ions with a linear response range in the micro-molar range. Finally, the utilization of the parallel microtiter plate approach allowed an accelerated evaluation of these material properties and nicely demonstrates the advantages of combinatorial approaches in materials science.[24]

We would like to thank the Dutch Polymer Institute (Project #360) for financial support.

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