

# Prussian Blue Nanocontainers: Selectively Permeable Hollow Metal–Organic Capsules from Block Ionomer Emulsion-Induced Assembly

Xavier Roy,<sup>†</sup> Joseph K.-H. Hui,<sup>†</sup> Muhammad Rabnawaz,<sup>‡</sup> Guojun Liu,<sup>‡</sup> and Mark J. MacLachlan<sup>\*,†</sup>

<sup>†</sup>Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, British Columbia, Canada V6T 1Z1

<sup>‡</sup>Department of Chemistry, Queen's University, 90 Bader Lane, Chernoff Hall, Room 411, Kingston, Ontario, Canada K7L 3N6

**S** Supporting Information

**ABSTRACT:** Hollow polymer-based particles are useful for the encapsulation, protection, and release of active compounds. Adding a metal–organic coordination framework shell to nanocontainers is an attractive goal because it should help control their stability and permeability while yielding new properties and functions. We have discovered that polymer capsules with a Prussian blue analogue inner shell can be synthesized by emulsion-induced assembly of a metal-containing amphiphilic block ionomer. The capsules are selectively permeable and were used as nanocontainers to encapsulate and release a model compound. Further, these nanomaterials are tunable in size and organize into 2-D close-packed arrays in the solid state. Potential applications for these materials include the encapsulation and nanopatterning of pharmaceutical, biological, and catalytic compounds.

Metallopolymers were reported as early as 1955,<sup>1</sup> but progress in this field was slow until the 1990s, when improved synthetic methods were developed to access soluble, characterizable, and processable macromolecules.<sup>2</sup> Metal-containing block copolymers are especially advantageous because they can be made to assemble into a variety of inorganic nanostructures.<sup>3–7</sup> In particular, these have been used as precursors for ceramics,<sup>8,9</sup> for self-assembled nanolithography,<sup>10,11</sup> and in the synthesis and patterning of nanoparticles and metal clusters.<sup>11,12</sup>

Organic block copolymers have been extensively investigated as functional nanocontainers to encapsulate, protect, and release active compounds.<sup>13–15</sup> Cross-linking the polymer shells is important because it confers stability and controlled permeability to the aggregates.<sup>16,17</sup> New properties and functions have been achieved by incorporating inorganic species inside the walls of block copolymer vesicles<sup>18,19</sup> and other types of nanocapsules.<sup>20,21</sup> However, we have found no report of hollow nanostructures made of coordination frameworks. Materials of this type are attractive because they possess controllable microporosities, high surface areas, good mechanical and thermal stabilities, and exciting electronic and magnetic properties.<sup>22–25</sup> A few guest compounds have been included within solid coordination framework nanoparticles, and these have been investigated for drug delivery and light harvesting.<sup>26–28</sup> Accessing hollow coordination frameworks could significantly broaden the range of active compounds that can be encapsulated.

Prussian blue analogues (PBAs) are a family of metal–organic coordination frameworks constructed from metal ions bridged by cyanide ligands.<sup>25</sup> Nanomaterials have been constructed from PBAs through a variety of approaches.<sup>29–34</sup> PB has been intercalated into surfactant multilayer vesicles that were immobilized within a polymer matrix,<sup>35</sup> and it has been polymerized on the periphery of block copolymer micelles.<sup>36,37</sup> Unfortunately, in the latter case, hollow nanostructures could not be accessed by removal of the organic core.

Oil-filled organic nanocapsules have been prepared by emulsion-induced assembly of a triblock copolymer,<sup>38</sup> but, to the best of our knowledge, this technique has never been applied to metal-containing block copolymers.

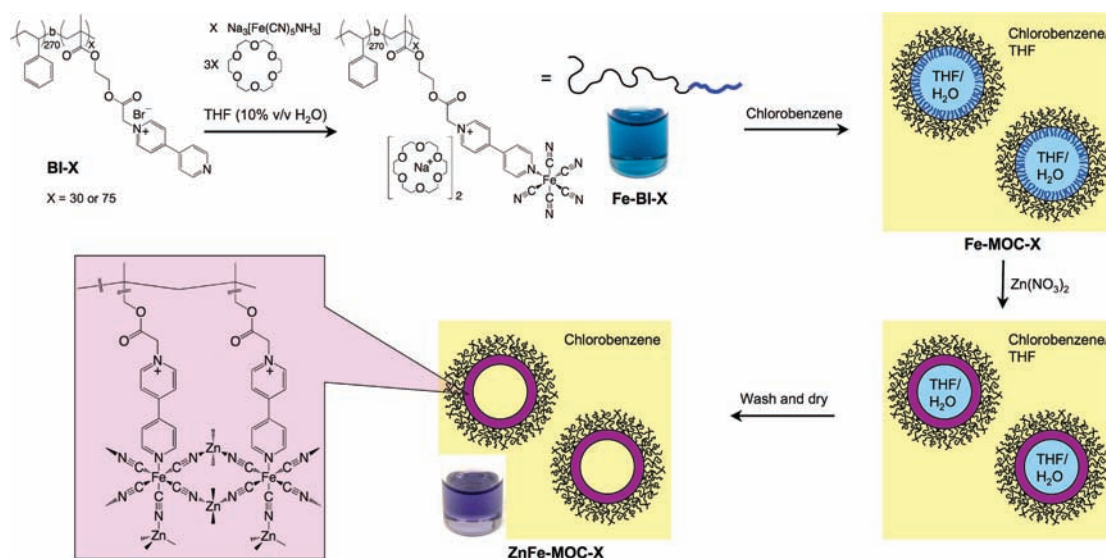
Recently, we described the synthesis and self-assembly of a novel metal cyanide block ionomer that can be cross-linked into worm-shaped PBA frameworks.<sup>34</sup> Here, we use similar metal-containing block ionomers to fabricate soluble metal–organic capsules (MOCs) made of a PBA through emulsion-induced assembly. We also report the encapsulation of methylene blue, a dye molecule, inside the structures.

Our approach to PBA capsules is illustrated in Figure 1. We first synthesized the two block ionomers, **BI-30** and **BI-75**. They had one segment of 270 styrene units and another segment of 30 and 75 monoquaternized 4,4'-bipyridinium-functionalized 2-hydroxyethyl methacrylate units, respectively. **BI-30** and **BI-75** were then reacted with Na<sub>3</sub>[Fe(CN)<sub>5</sub>NH<sub>3</sub>] and 18-crown-6 in THF (10% v/v H<sub>2</sub>O) to yield the pentacyanoferrate(II) block ionomers **Fe-BI-30** and **Fe-BI-75**, respectively. The deep blue materials are soluble in THF, benzene, toluene, and most halogenated solvents.

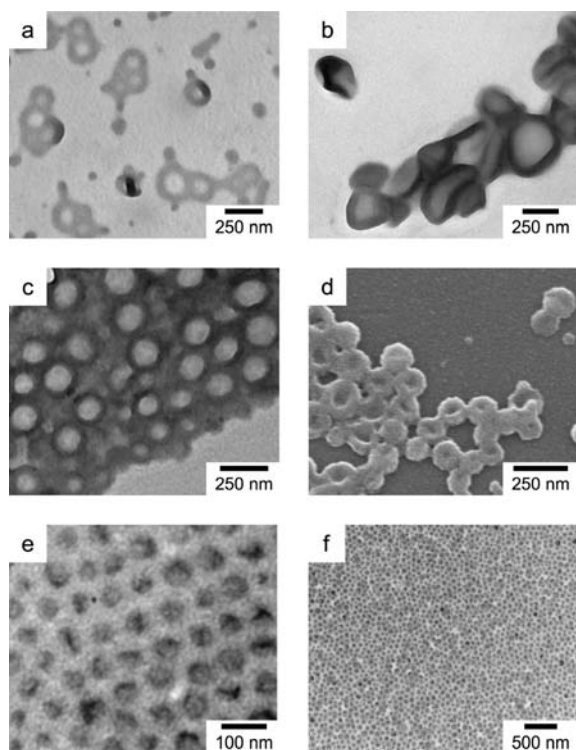
Addition of chlorobenzene to the stirring THF (10% v/v H<sub>2</sub>O) mixtures induces a water-in-oil emulsion, which is promptly stabilized by **Fe-BI-30** or **Fe-BI-75** present in solution. We expected the amphiphilic macromolecules to position themselves at the water–oil interface of nanosized water droplets and prevent the dispersed aqueous phase from coalescing. We added Zn(NO<sub>3</sub>)<sub>2</sub> in THF to the emulsion to cross-link the [Fe(CN)<sub>5</sub>]<sup>3–</sup>-containing shells into PBA-type frameworks.<sup>39</sup> THF was finally removed from the organic phase by aqueous extraction. The solvent-filled capsules **ZnFe-MOC-30** and **ZnFe-MOC-75** were obtained as clear burgundy chlorobenzene solutions upon standing over activated molecular sieves. A polystyrene

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**Figure 1.** Synthetic approach to soluble block ionomer–PBA capsules through emulsion-induced assembly. Photographs of **Fe-BI-75** and **ZnFe-MOC-75** are included as a visual reference for the color change.



**Figure 2.** Microscopy characterization of the polymer aggregates. (a) TEM micrograph of the Zn-cross-linked **Fe-BI-75** nanoring structures observed before the emulsion-induced assembly. (b,c) TEM micrographs of the deformed **Fe-MOC-75** and the **ZnFe-MOC-75** hollow aggregates, respectively. (d) SEM micrograph showing a mixture of partially and fully collapsed hollow capsules for **ZnFe-MOC-75**. (e) High- and (f) low-magnification TEM micrographs of **ZnFe-MOC-30**.

corona renders the cross-linked spheres soluble in many organic solvents, including chlorobenzene, benzene, toluene, THF, and chlorinated hydrocarbons.

In THF (10% v/v H<sub>2</sub>O), **Fe-BI-30** and **Fe-BI-75** assemble into nanoworms and nanorings, respectively. Figure 2a shows the

Zn-cross-linked **Fe-BI-75** nanorings obtained by drop-casting on a transmission electron microscopy (TEM) grid. A small proportion of spherical micelles and short nanoworms is also typically observed. Figure 2b shows the unlinked **Fe-MOC-75** materials formed by emulsion-induced assembly. The micrograph suggests that these are deformed hollow capsules. Circular nanostructures are observed after cross-linking the [Fe(CN)<sub>5</sub>]<sup>3-</sup> terminal groups with Zn<sup>2+</sup> (Figure 2c), which is consistent with a more rigid inner shell.

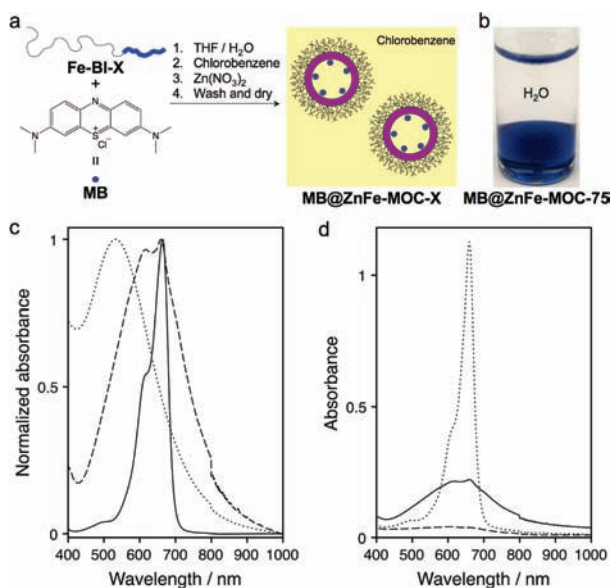
We used scanning electron microscopy (SEM) and atomic force microscopy (AFM) to confirm that the aggregates are indeed round and hollow. A mixture of partially and fully collapsed spherical capsules is observed by SEM for **ZnFe-MOC-75** in Figure 2d. Topographic and height profile images of isolated capsules were obtained for **Fe-MOC-75** and **ZnFe-MOC-75** (see Supporting Information (SI)) and verify that the aggregates are not toroids. These AFM results are consistent with the polymeric materials being pseudo-spherical capsules with a collapsed hollow core.

The capsules are stable for days in solution, as confirmed by TEM, and can even be diluted in THF/water mixtures without any observable morphology change.

The average inner diameter of the spheres for **ZnFe-MOC-75** is 137 ± 43 nm. Figure 2e,f shows that smaller and nearly monodisperse hollow capsules (53 ± 5 nm) are obtained for **ZnFe-MOC-30** by sonicating **Fe-MOC-30** before cross-linking. Figure 2e suggests that **ZnFe-MOC-30** may be assembling into a close-packed array upon solvent evaporation. Fast Fourier transform (FFT) analysis of the low-magnification image in Figure 2f reveals that the frequency spots distribute in a circular band. This implies a close-packed superlattice with no single domain of organization.

We were able to image **Fe-MOC-75** hollow structures prepared around the solution cloud point (~78% v/v THF, 15% v/v chlorobenzene, 7% v/v H<sub>2</sub>O; SI, Figure S10). This result also supports an emulsion-induced mechanism for the formation of the capsules.

In chlorobenzene, **Fe-MOC-75** is purple owing to a metal-to-ligand charge-transfer transition centered at ~600 nm (SI, Figure S4).



**Figure 3.** Encapsulation inside block ionomer–PBA capsules. (a) The synthetic approach to encapsulating the model compound **MB** inside the aggregates. (b) Photograph of **MB@ZnFe-MOC-75** in chlorobenzene after stirring with water for 24 h. (c) UV–vis absorption spectra of **MB** in water (solid line), and **MB@ZnFe-MOC-75** (dashed line) and **ZnFe-MOC-75** (dotted line) in chlorobenzene. The absorbances were normalized to facilitate comparison between the spectra. (d) UV–vis absorption spectra of **MB@ZnFe-MOC-75** in pure chlorobenzene (solid line), in chlorobenzene with 25% v/v MeOH (dotted line), and in chlorobenzene after extraction of the MeOH (dashed line).

This band, still present for **ZnFe-MOC-75**, is blue-shifted by 70 nm (relative to **Fe-MOC-75**) to  $\sim 530$  nm after addition of  $\text{Zn}^{2+}$ , confirming that the  $[\text{Fe}(\text{CN})_5]^{3-}$  complex is still coordinated to the block ionomer. These data support the conversion of the block ionomer-tethered iron cyanide complexes into an extended PBA-type metal–organic coordination framework.<sup>32,34</sup> Similar transitions were measured for **ZnFe-MOC-30**.

Further evidence for the connectivity of the PBA network was obtained by IR spectroscopy and energy-dispersive X-ray analysis (EDX) of the solid materials. IR spectra of the different polymer aggregates consistently show peaks attributable to both organic blocks and the pentacyanoferrate(II) complex. Of particular interest is the energy of the  $\nu_{\text{CN}}$  stretching band, which is diagnostic of the coordination environment for the iron cyanide complex. The approximately  $C_{4v}$ -symmetric precursor  $\text{Na}_3[\text{Fe}(\text{CN})_5\text{NH}_3]$  exhibits three  $\nu_{\text{CN}}$  stretching modes, with the strongest band at  $2030\text{ cm}^{-1}$ . Exchanging the amine with the strong  $\pi$ -accepting 4,4'-bipyridinium ligand upon complexation of the block ionomer results in a  $20\text{ cm}^{-1}$  blue shift for the  $\nu_{\text{CN}}$  stretching mode to  $2050\text{ cm}^{-1}$ . Cross-linking **Fe-MOC-30** and **Fe-MOC-75** into zinc–iron cyanide framework shells broadens and shifts the  $\nu_{\text{CN}}$  stretching band to even higher energies ( $2078\text{--}2082\text{ cm}^{-1}$ ). This broadening and blue shift is a well-established trend for cyanide ligands switching from a terminal mode to a bridging one, as expected for the formation of PBA-type frameworks.<sup>40,41</sup> In addition, EDX confirmed the incorporation of both Zn and Fe in the polymer aggregates.

Able to reproducibly prepare cross-linked MOCs, we next investigated the encapsulation of methylene blue (**MB**), a prototypical water-soluble compound (Figure 3a). We selected the charged organic molecular dye **MB** because it has an easily

recognizable solution absorption band at  $\sim 650$  nm (Figure 3c). An aqueous solution of **MB** was first added to **Fe-BI-30** or **Fe-BI-75** in THF (10% v/v  $\text{H}_2\text{O}$ ), followed by chlorobenzene addition to induce the water-in-oil emulsion. The solvent-filled aggregates were then cross-linked with  $\text{Zn}(\text{NO}_3)_2$ , and the non-encapsulated **MB** was extracted by washing the organic phase with water until no blue color was observed in the aqueous phase. **MB@ZnFe-MOC-30** and **MB@ZnFe-MOC-75** were obtained as clear blue chlorobenzene solutions upon standing over activated molecular sieves.

Figure 3c shows the normalized UV–vis absorption spectra for **ZnFe-MOC-75** and **MB@ZnFe-MOC-75**. In the latter spectrum, the much stronger absorption of **MB** overwhelms that of **ZnFe-MOC-75**, and only absorptions due to **MB** are observed in the range 500–800 nm. The band is much broader and has a different shape when compared with that of **MB** in aqueous solution. The absorption spectrum is, in fact, analogous to the one measured for a **MB** film deposited on a silica surface.<sup>42</sup> **MB** most likely precipitates inside the capsules during the encapsulation process, and a broad solid absorption spectrum is recorded.

We also explored the possibility that **MB** might be trapped inside the PBA network or precipitated within the polystyrene corona and not actually encapsulated inside the capsule. As a control experiment, we first cross-linked **Fe-BI-75** with  $\text{Zn}(\text{NO}_3)_2$  in the presence of **MB** and then induced the water-in-oil emulsion with chlorobenzene. After thorough washing, we verified by TEM that nanoring structures were obtained and confirmed that no **MB** was observed by UV–vis absorption spectroscopy.

**MB@ZnFe-MOC-75** and **MB@ZnFe-MOC-30** (in chlorobenzene) can be stirred with water for days with no transfer of the blue color into the aqueous phase (Figure 3b). Furthermore, we detected no change in the absorption spectrum, indicating that water does not cross the hydrophobic polystyrene corona to solvate **MB**.

A different behavior is obtained with methanol, which rapidly and noticeably changes the color of the **MB@ZnFe-MOC-75** and **MB@ZnFe-MOC-30** solutions (Figure 3d). A narrower and much more intense absorption band is observed after the addition of 25% v/v MeOH to **MB@ZnFe-MOC-75** in chlorobenzene (dotted line) when compared with the pure chlorobenzene solution (solid line). The spectrum for the methanol/chlorobenzene solvent mixture is very similar to the **MB** solution spectrum and suggests that methanol molecules can cross the polystyrene and zinc–iron cyanide framework barriers and solvate **MB** inside the capsules. TEM confirmed that the majority of the hollow structures remained intact after addition of methanol, although we observed that some ruptured, probably due to rapid uptake of methanol into the core. The methanol was extracted from the organic phase by washing with water, and a blue aqueous phase was obtained. The UV–vis spectrum of **MB@ZnFe-MOC-75** in chlorobenzene after extraction of the methanol shows that most of the **MB** was removed from within the capsules in the process (dashed line; only a very weak **MB** solid-state transition is observed). Thus, the dye can be selectively released from the MOCs with methanol but not with water.

In summary, we report the first example of soluble PBA-type capsules and the encapsulation of a water-soluble model compound in its core. We stabilized a water-in-oil emulsion with an assembled iron cyanide block ionomer that we cross-linked into a metal–organic framework. The nanoscale hollow aggregates are tunable in size, are stable in solution for days, show selective

permeability and release capability, and assemble into close-packed superlattices on surfaces. These nanomaterials could be useful to encapsulate and nanopattern active compounds for applications such as drug delivery, sensor arrays, and catalyst immobilization and organization. In addition, based on the diversity of the PBA family, we envision that this approach will provide a convenient route to capsules with tunable magnetic, optical, and electronic properties.

## ■ ASSOCIATED CONTENT

**S Supporting Information.** Experimental details and additional characterization. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## ■ AUTHOR INFORMATION

**Corresponding Author**  
mmaclach@chem.ubc.ca

## ■ ACKNOWLEDGMENT

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## ■ REFERENCES

- (1) Arimoto, F. S.; Haven, A. C., Jr. *J. Am. Chem. Soc.* **1955**, *77*, 6295.
- (2) Abd-El-Aziz, A. S.; Manners, I. *Frontiers in Metal-Containing Polymers*; Wiley: Hoboken, NJ, 2007.
- (3) Ni, Y.; Rulkens, R.; Manners, I. *J. Am. Chem. Soc.* **1996**, *118*, 4102.
- (4) Beck, J. B.; Rowan, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 13922.
- (5) Andres, P. R.; Schubert, U. S. *Adv. Mater.* **2004**, *16*, 1043.
- (6) Fiore, G. L.; Klinkenberg, J. L.; Fraser, C. L. *Macromolecules* **2008**, *41*, 9397.
- (7) Gilroy, J. B.; Gädt, T.; Whittell, G. R.; Chabanne, L.; Mitchels, J. M.; Richardson, R. M.; Winnik, M. A.; Manners, I. *Nature Chem.* **2010**, *2*, 566.
- (8) Clendenning, S. B.; Han, S.; Coombs, N.; Paquet, C.; Rayat, M. S.; Grozea, D.; Brodersen, P. M.; Sodhi, R. N. S.; Yip, C. M.; Lu, Z.-H.; Manners, I. *Adv. Mater.* **2004**, *16*, 291.
- (9) Malenfant, P. R. L.; Wan, J.; Taylor, S. T.; Manoharan, M. *Nature Nanotechnol.* **2007**, *2*, 43.
- (10) Cheng, J. Y.; Ross, C. A.; Chan, V. Z.-H.; Thomas, E. L.; Lammertink, R. G. H.; Vancso, G. J. *Adv. Mater.* **2001**, *13*, 1174.
- (11) Glass, R.; Möller, M.; Spatz, J. P. *Nanotechnology* **2003**, *14*, 1153.
- (12) Chakraborty, S.; Keightley, A.; Dusevich, V.; Wang, Y.; Peng, Z. *Chem. Mater.* **2010**, *22*, 3995.
- (13) Gu, F.; Zhang, L.; Teply, B. A.; Mann, N.; Wang, A.; Radovic-Moreno, A. F.; Langer, R.; Farokhzad, O. C. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 2586.
- (14) Klalkherd, A.; Nagamani, C.; Thayumanavan, S. *J. Am. Chem. Soc.* **2009**, *131*, 4830.
- (15) Discher, D. E.; Eisenberg, A. *Science* **2002**, *297*, 967.
- (16) Rösler, A.; Vandermeulen, G. W. M.; Klok, H.-A. *Adv. Drug Delivery Rev.* **2001**, *53*, 95.
- (17) Wang, H.; Wang, X.; Winnik, M. A.; Manners, I. *J. Am. Chem. Soc.* **2008**, *130*, 12921.
- (18) Mai, Y.; Eisenberg, A. *J. Am. Chem. Soc.* **2010**, *132*, 10078.
- (19) Metera, K. L.; Sleiman, H. *Macromolecules* **2007**, *40*, 3733.
- (20) Katagiri, K.; Hamasaki, R.; Ariga, K.; Kikuchi, J.-i. *Langmuir* **2002**, *18*, 6709.
- (21) Vasquez, Y.; Sra, A. K.; Schaak, R. E. *J. Am. Chem. Soc.* **2005**, *127*, 12504.
- (22) Kitagawa, S.; Kitaura, R.; Noro, S.-i. *Angew. Chem. Int. Ed.* **2004**, *43*, 2334.
- (23) Harbuzaru, B. V.; Corma, A.; Rey, F.; Atienzar, P.; Jordá, J. L.; Garcia, H.; Ananias, D.; Carlos, L. D.; Rocha, J. *Angew. Chem. Int. Ed.* **2008**, *47*, 1080.
- (24) Wang, B.; Côté, A. P.; Furukawa, H.; O'Keefe, M.; Yaghi, O. M. *Nature* **2008**, *453*, 207.
- (25) Shatruk, M.; Avendano, C.; Dunbar, K. R. *Prog. Inorg. Chem.* **2009**, *56*, 155.
- (26) Rieter, W. J.; Pott, K. M.; Taylor, K. M. L.; Lin, W. *J. Am. Chem. Soc.* **2008**, *130*, 11584.
- (27) Zhang, X.; Ballem, M. A.; Ahrén, M.; Suska, A.; Bergman, P.; Uvdal, K. *J. Am. Chem. Soc.* **2010**, *132*, 10391.
- (28) Carné, A.; Carbonell, C.; Imaz, I.; MasPOCH, D. *Chem. Soc. Rev.* **2011**, *40*, 291.
- (29) Vaucher, S.; Li, M.; Mann, S. *Angew. Chem. Int. Ed.* **2000**, *39*, 1793.
- (30) Zhou, P.; Xue, D.; Luo, H.; Chen, X. *Nano Lett.* **2002**, *2*, 845.
- (31) Uemura, T.; Kitagawa, S. *J. Am. Chem. Soc.* **2003**, *125*, 7814.
- (32) Roy, X.; Thompson, L. K.; Coombs, N.; MacLachlan, M. J. *Angew. Chem. Int. Ed.* **2008**, *47*, 511.
- (33) Lepoutre, S.; Grosso, D.; Sanchez, C.; Fornasieri, G.; Rivière, E.; Bleuzen, A. *Adv. Mater.* **2010**, *22*, 3992.
- (34) Roy, X.; Hui, J. K.-H.; Rabnawaz, M.; Liu, G.; MacLachlan, M. J. *Angew. Chem. Int. Ed.* **2011**, *50*, 1597.
- (35) Einaga, Y.; Sato, O.; Iyoda, T.; Fujishima, A.; Hashimoto, K. *J. Am. Chem. Soc.* **1999**, *121*, 3745.
- (36) Liang, G.; Xu, J.; Wang, X. *J. Am. Chem. Soc.* **2009**, *131*, 5378.
- (37) McHale, R.; Ghasdian, N.; Liu, Y.; Ward, M. B.; Hondow, N. S.; Wang, H.; Miao, Y.; Brydson, R.; Wang, X. *Chem. Commun.* **2010**, *46*, 4574.
- (38) Zheng, R.; Liu, G. *Macromolecules* **2007**, *40*, 5116.
- (39) We selected zinc ferrocyanide as our model compound because its porous framework efficiently promotes diffusion of small species and it lacks a charge-transfer band that limits spectroscopic investigation of encapsulated dye. See: Cartraud, P.; Cointot, A.; Renaud, A. *J. Chem. Soc., Faraday Trans. 1* **1981**, *77*, 1561.
- (40) Nakamoto, K. *Infrared Spectra of Inorganic and Coordination Compounds*; John Wiley & Sons: New York, 1963.
- (41) Kettle, S. F. A.; Diana, E.; Boccaleri, E.; Stanghellini, P. L. *Inorg. Chem.* **2007**, *46*, 2409.
- (42) Li, F.; Zare, R. N. *J. Phys. Chem. B* **2005**, *3330*.