Iron porphyrins anchored to a thermosensitive polymeric core-shell nanosphere as a thermotropic catalyst†

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Received (in Cambridge, UK) 1st February 2005, Accepted 12th April 2005
First published as an Advance Article on the web 29th April 2005
DOI: 10.1039/b501515d

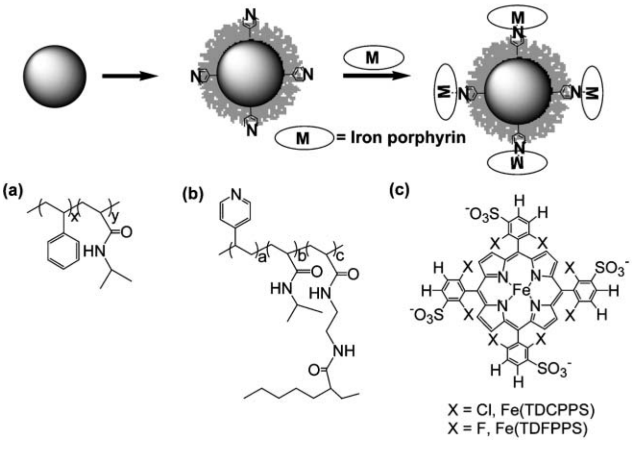
A thermosensitive nanocatalyst was prepared in the reaction of water-soluble iron(III) porphyrins and thermosensitive polymeric nanospheres with a core-shell structure; its catalytic activity in cyclohexene oxidation by iodosylbenzene was dependent markedly on reaction temperatures in aqueous solution.

The poly(*N*-isopropylacrylamide) (NIPAAm) undergoes random coil to globule transition at temperatures above its lower critical solution temperature (LCST) in aqueous solution; it is hydrophilic and has an extended conformation below its LCST, whereas it becomes hydrophobic and adopts a collapsed conformation above its LCST.[1,2] Based on the thermosensitive properties, NIPAAm homo- and copolymers have been widely used in the applications of drug delivery,[3] separation,[4] cell culture,[5] and artificial cell preparation.[6]

The use of metalloporphyrins as catalysts in oxygenation reactions has been extensively investigated in biomimetic studies as well as in industrial applications.[7–9] In particular, there have been a number of reports on heterogeneous catalytic oxygenation systems, in which metalloporphyrin catalysts are immobilized on soluble or insoluble polymer supports such as surface-modified mesoporous silica, Merrifield's resins, and highly cross-linked polymers.[10–13] Responsive polymer supports that are sensitive to temperature and/or pH changes have been also reported.[14] Recently, micro-to-nano scaled particles have been reported for the design of a self-healing polymer, or a novel catalyst that shows chemical activities different from those immobilized onto supports.[15–17] We therefore prepared an iron porphyrin catalyst coordinated to thermosensitive core-shell nanospheres (**1**) and investigated its catalytic activity as a function of reaction temperature in cyclohexene oxidation by iodosylbenzene (PhIO) in aqueous solution, with an expectation that each nanosphere of iron porphyrin catalyst can act as a hydrophobic center for the organic substrate and the oxidant above its LCST in aqueous solution, and can be recycled by centrifugation after the reaction. In addition, the nanosphere catalyst has a high surface to volume ratio, providing an effective contact with the substrate and oxidant.

The core-shell nanospheres were prepared by a method similar to those reported elsewhere.[18,19] The core, consisting of poly(styrene-*co*-*N*-isopropylacrylamide), shows a structural rigidity in the reaction medium (Scheme 1a). The shell, consisting of poly(*N*-isopropylacrylamide-*co*-vinyl pyridine), functions as a linker to bind iron porphyrin complexes (Scheme 1b). Furthermore, pyridine bound to metalloporphyrins as an axial ligand has shown to increase the catalytic activity of metalloporphyrin catalysts.[20–22] Water-soluble iron(III) porphyrins that have shown catalytic activities in aqueous reactions previously,[23] such as the sodium salt of 5,10,15,20-tetrakis(2,6-difluoro-3-sulfonatophenyl)porphinato iron(III) $[\mathrm{Fe(TDFPPS)}]^{3+}$ or the sodium salt of 5,10,15,20-tetrakis(2,6-dichloro-3-sulfonatophenyl)porphinato iron(III) $[\mathrm{Fe(TDCPPS)}]^{3+}$ (Scheme 1c), were attached to nanospheres, giving thermosensitive polymer-supported nanocatalysts **1**. The core-shell nanospheres without a pyridinyl group did not bind the iron porphyrin catalyst. The loading of metalloporphyrins on the core-shell nanospheres was determined by monitoring the disappearance of a Soret band (see ESI, Fig. S1†). Based on the decrease of the Soret band, the amount of iron porphyrin catalyst in **1** was calculated to be 0.014 mmol per 1.0 g of polymer. The scanning electron microscope image of **1** shows well-shaped nanospheres with a uniform size of 480 nm (Fig. 1).

The LCST of the nanospheres in water was determined with a UV-vis spectrophotometer, by following the absorbance change at 500 nm (Fig. 2).[24] The high absorbance at 500 nm below 30 °C was an indication of a stable suspension of the nanospheres in water. Above the LCST (*i.e.*, 40 °C), most of nanospheres were aggregated to sink down below the light path in the cell, giving a low absorbance at 500 nm. A few residual floating nanospheres in solution contribute to the absorbance at 500 nm above 40 °C. In addition, when the relative size of a nanosphere was determined by dynamic light scattering as a function of temperature in water, the



Scheme 1 Synthetic scheme of an iron porphyrin-bound nanosphere, and structures of (a) core, (b) shell, and (c) iron porphyrins.

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† Electronic supplementary information (ESI) available: experimental details and Figs. S1–S2. See http://www.rsc.org/suppdata/cc/b5/b501515d/
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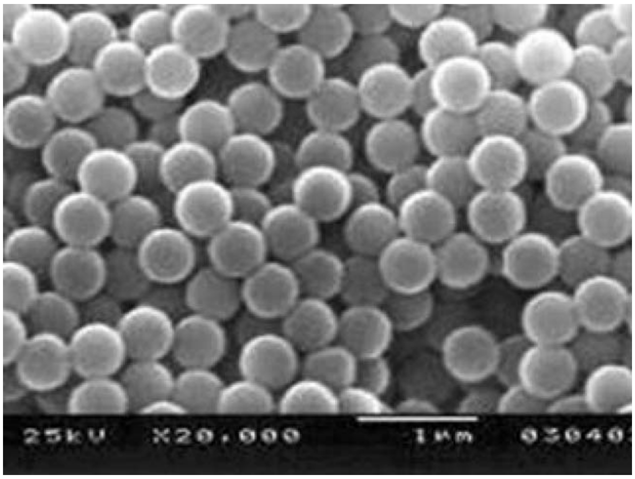

Fig. 1 Scanning electron microscope image of iron porphyrin-bound core-shell nanospheres **1**.

nanosphere diameter decreased from 480 nm to 350 nm as the temperature increased from 20 to 40 °C (see ESI, Fig. S2†). This result indicates that the swelling decreases due to a thermal transition of the temperature-sensitive shell.

To evaluate the thermosensitive catalytic activity of **1**, the oxidation of cyclohexene by PhIO was performed at different temperatures in aqueous solution. The results shown in Fig. 2 demonstrate that the conversion of cyclohexene to its corresponding epoxide was high (~70% yield based on cyclohexene used) at the transition temperature of 30–40 °C. Below the LCST and above the LCST of the nanocatalyst **1**, the product yields decreased markedly. To understand the mechanism of the above catalytic activity, a series of control experiments were performed. First, the oxidation of cyclohexene with the homogeneous iron porphyrin [Fe(TDFPPS)] and PhIO gave low product yield (*e.g.*, ~13%) irrespective of reaction temperatures. Second, the addition of pyridine (an equivalent amount of polymeric pyridine in **1**) to the above control experiment gave a marginal increase (~6.0%) in the yield. Third, the oxidation of cyclohexene with PhIO without catalyst did not give any products. Fourth, the experiment using PhIO and core-shell nanospheres with no anchored iron porphyrin did not give any products either. These control experiments demonstrate that the cyclohexene oxidation was carried out by the iron porphyrins anchored to the polymeric core-shell nanospheres. Further, the significant increase in the yield, from 20% to 70%, by **1** around the LCST might be related to the change in the hydrogel state, followed by a change in the partitioning and localization of the reagent to the nanospheres. To support this hypothesis, the partition coefficient of the cyclohexene to the nanospheres against water (K = $[\text{cyclohexene}]_{\text{nanospheres}}/[\text{cyclohexene}]_{\text{water}}$) = ($\{[\text{cyclohexene}]_{\text{total}} - [\text{cyclohexene}]_{\text{water}}\}/[\text{cyclohexene}]_{\text{water}}$) was measured as a function of temperature. The experimental protocol is added in the ESI.† The partition coefficient to the nanospheres was measured as a function of temperature in a range of 15 °C–50 °C. The partition coefficient increased from 2.5 (±0.1)–2.6 (±0.1) below 25 °C to 3.3 (±0.2) at 30 °C. At 40 °C or higher temperature, the cyclohexene was squeezed out of the nanospheres due to the dense shrinkage of the nanospheres, resulting in the decrease in the partition coefficient to 2.7 (±0.2). The squeezing of the poly(NIPAAm) hydrogel followed by indomethacin release was reported in the temperature sensitive drug delivery system.[25] When the surface is hydrophobic at temperatures around its LCST, the hydrophobic substrates are absorbed in the nanospheres, resulting in the increase in the local concentration of the substrate. At higher temperatures, the surface becomes densely shrunken. This might not only interfere with the catalytic activity of the anchored iron porphyrin but also decrease the permeabilities of the reactants. At lower temperatures, the hydrophobic reactant has less chance to come into contact with **1** due to the hydrophilic nature of the shell. Therefore, the product yield was maximal at and around the transition temperature (Fig. 2). The maximal activity for allyl alcohol hydrogenation at LCST in water was reported for a poly(NIPAAm) protected gold–platinum nanoparticle catalyst. Below the LCST, the reactivity followed Arrhenius-type kinetics, whereas the activity decrease at 40 °C was due to the phase separation of the catalyst and hydrophilic allyl alcohol.[26,27]

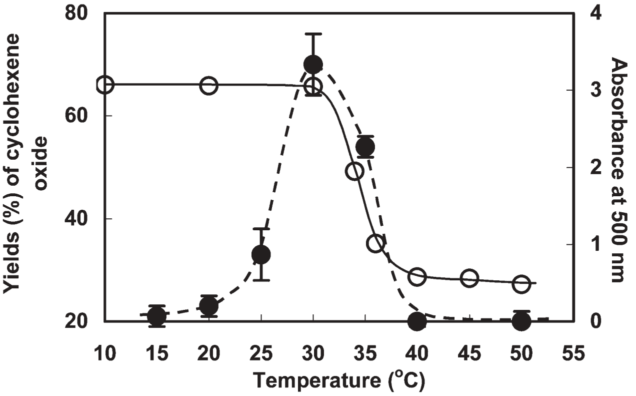

Fig. 2 The absorbance change at 500 nm indicates that the LCST of the nanoparticles in water (1.5 wt/vol%) is at 30–40 °C (○). The yields of cyclohexene oxide are shown as a function of temperature in water (●). The product yields are an average of triplicate experiments, and standard deviations are indicated by error bars.

The recyclability of the nanocatalyst (**1**) was then examined in cyclohexene oxidation by PhIO in a solvent mixture of acetonitrile and water (*v*/*v* = 1 : 1). A high yield of cyclohexene oxide was produced with trace amounts of 2-cyclohexen-1-ol and 2-cyclohexen-1-one (81% yield based on cyclohexene added). We therefore carried out the recycling experiment and found that 89% and 83% of the initial activity was maintained in the second and third trials, respectively (see ESI, Experimental Section†). This result indicates that the recovered nanocatalyst did not lose much of its catalytic activity. Further, by taking UV-vis spectra of reaction solutions, the amount of leached iron porphyrin was found to be negligible during catalytic reactions.

It has been shown previously that microenviromental control leads to the optimum conditions for a chemical reaction. For example, the hydrolysis rate of *p*-nitrophenyl esters showed a maximal reactivity in a solvent composition of 12–35 vol% (ethanol–water) due to the appropriate hydrophobic environment in the solvent mixture.[28] Thermosensitive micelles of poly(ethylene oxide-b-propylene oxide-b-ethylene oxide) showed enhanced oxidation rates for the conversion of methyl *p*-tolyl sulfide to methyl *p*-tolyl sulfoxide.[29] The product yields in the Suzuki coupling reaction between aryl halides and aryl boronic acids were increased using a micelle composed of a core of hydrophobic hexa-*p*-phenylene rods and a hydrophilic poly(ethylene glycol) shell, because the confinement of the aromatic substrates by the rod bundle increases the π–π interactions in water.[30] In our system, the temperature-sensitive hydrophobic transition seems to provide the optimal environment for the oxidation of the cyclohexene.

In conclusion, a thermosensitive heterogeneous catalyst was prepared by anchoring iron porphyrin complexes to thermosensitive core-shell nanospheres. The nano-sized catalyst showed a maximum catalytic activity in cyclohexene oxidation at and around the transition temperature of 30–40 °C, and this temperature effect was rationalized by the balance of swelling and hydrophobicity of the core-shell nanospheres.

This work was supported by the Korea Science and Engineering Foundation (Grant No: R01-2002-000-00274-0) and the Ministry of Science and Technology of Korea through Creative Research Initiative Program.

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