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Temperature-Sensitive Dendritic Hosts: Synthesis, Characterization, and Control of Catalytic Activity

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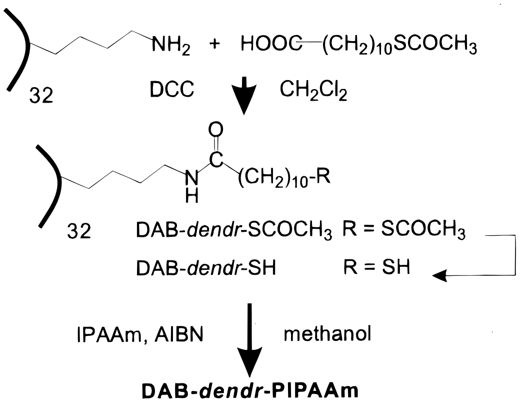
Dendrimers serve as supramolecular hosts due to their well-defined three-dimensional structures that possess internal nanoscopic cavities.[1] The internal cavities of dendrimers encapsulate organic and inorganic guests and provide a specific microenvironment for guest molecules.[2] Meijer et al. have reported the static encapsulation of guest molecules caused by the modification of the terminal groups of poly(propyleneimine)-dendrimers with amino acids.[3] This modification of terminal groups with stimulus-sensitive groups allows for the control of guest reactivity in the dendritic host in response to the changes of external stimuli.[4]

Poly(*N*-isopropylacrylamide) (PIPAAm) exhibits temperature-dependent solubility in aqueous media with the lower critical solution temperature (LCST).[5] PIPAAm and its cross-linked PIPAAm hydrogel have been extensively investigated for their potential in several applications including drug-delivery devices, chemical valves, and actuators in response to temperature change.[6] Bergbreiter et al. have reported "smart" polymer-bound catalysts using temperature-sensitive polymeric ligands.[7] Herein, we report on the synthesis of temperature-sensitive dendritic hosts by reacting the thiol terminal groups of the modified poly(propyleneimine)dendrimer with *N*-isopropylacrylamide (IPAAm). Dendrimer-based multiarm copolymers have been reported by several researchers.[8] We also find that the dendrimer-based copolymer with temperature-sensitive arms causes marked changes in catalytic activity for a guest catalyst in water in response to a temperature change.

The temperature-sensitive dendritic host (DAB-*dendr*-PIPAAm) is constructed from a third generation poly(propyleneimine) dendrimer that possesses 32 primary amine end groups (Scheme 1). The primary amine terminal groups were reacted with 11-(thioacetyl)undecanoic acid in CH_2Cl_2 in the presence of dicyclohexylcarbodiimide (DCC). The amidated dendrimer (DAB-*dendr*-$SCOCH_3$) was purified using gel permeation chromatography and was characterized by ^{1}H NMR, ^{13}C NMR, FTIR, DSC, size-exclusion chromatography (SEC), and MALDI−TOF−mass spectrometry (see Supporting Information). After hydrolysis of the thioacetyl groups, DAB-*dendr*-PIPAAm was synthesized by conducting a free-radical polymerization of IPAAm using 2, 2′-azobis(isobutyronitrile) (AIBN) and DAB-*dendr*-SH. The modified dendrimer DAB-*dendr*-SH was used as a chain transfer reagent for the radical polymerization of IPAAm in order to produce a dendrimer-based multiarm copolymer.

The formation of a DAB-*dendr*-PIPAAm with PIPAAm arms around the dendrimer surface was supported by ^{1}H NMR, SEC, a transmission electron micrograph (TEM), and dynamic light scattering (DLS).

Scheme 1



The ^{1}H NMR spectrum indicated that more than 90% of the thiol terminal groups were covalently attached with PIPAAm arms, with ca. 17 repeating IPAAm units per one arm. The purified DAB-*dendr*-PIPAAm did not contain an unreacted dendrimer according to SEC measurements. After treating DAB-*dendr*-PIPAAm with Cu^{2+}, TEM images revealed the presence of single spheriodal dendrimer molecules (Figure 1).[9] Their average diameter (1.9 nm) agreed with the estimated diameter of the third generation poly(propyleneimine) dendrimer. In addition, the average hydrodynamic diameter of DAB-*dendr*-PIPAAm was 11.7 ± 1.6 nm in water at 25 °C according to DLS measurement.

We encapsulated water-soluble cobalt(II) phthalocyanine complexes **1** and **2** into DAB-*dendr*-PIPAAm. Without DAB-*dendr*-PIPAAm, the visible spectra of **1** and **2** exhibited a broad Q-band around 618 nm. The shape of the Q-band absorption indicated that **1** and **2** existed as dimers or oligomers in water because of a strong stacking among hydrophobic phthalocyanine rings.[10] When DAB-*dendr*-PIPAAm was added, the spectrum of anionic **1** changed and a sharp peak at 688 nm was observed, which indicated that cobalt phthalocyanine was in a nonaggregated condition (Figure 2). On the other hand, the absorbance at 688 nm slightly increased in cationic **2**. Furthermore, the spectra of **1** remained virtually intact following the addition of the PIPAAm homopolymer and linear poly(ethylene imine) (M_w 600). The modified poly(propyleneimine) dendrimers with alkyl chains acted as dendritic hosts for anionic guest molecules such as Bengal Rose through electrostatic and hydrophobic interactions.[11] The appearance of this sharp peak suggests that DAB-*dendr*-PIPAAm affects the monomer−aggregate equilibrium of the anionic guest complex **1** by incorporation into the dendritic host through electrostatic complexation of negative carboxyl groups in **1** with the positive dendritic polymer as well as hydrophobic interaction between alkyl chains and phthalocyanine rings. The anionic guest **1** may be incorporated into the portion of the alkyl chains near the dendritic polymer in DAB-*dendr*-PIPAAm. This sorption of **1** within DAB-*dendr*-PIPAAm was irreversible: the absorption peaks of **1** were not observed in the filtrate from the ultrafilter (ADVANTEC USY-1).

Cobalt(II) phthalocyanines have been employed as effective catalysts for thiol oxidation.[12] This oxidation obeys the following equation, in which the consumption

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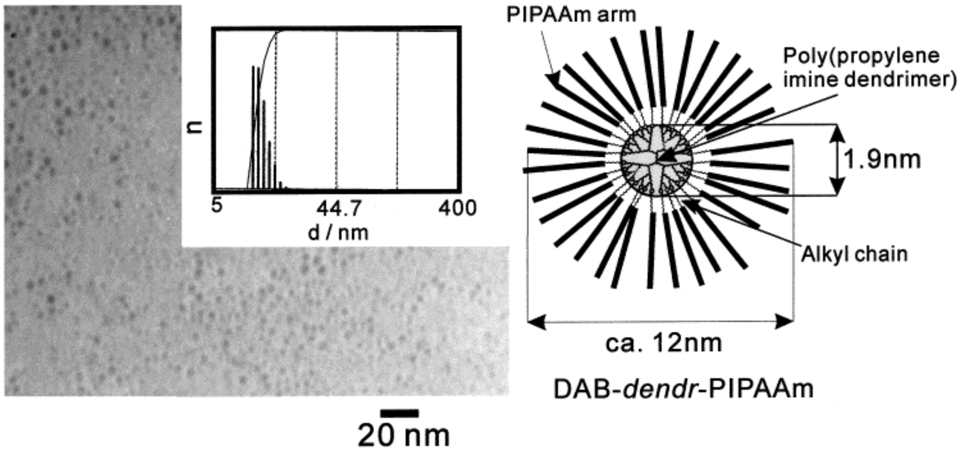

Figure 1. TEM image of DAB-*dendr*-PIPAAm with sorption of $CuSO_4$, showing the monodisperse size and shape distribution. Inset: DSL data of DAB-*dendr*-PIPAAm in water at 25 °C.

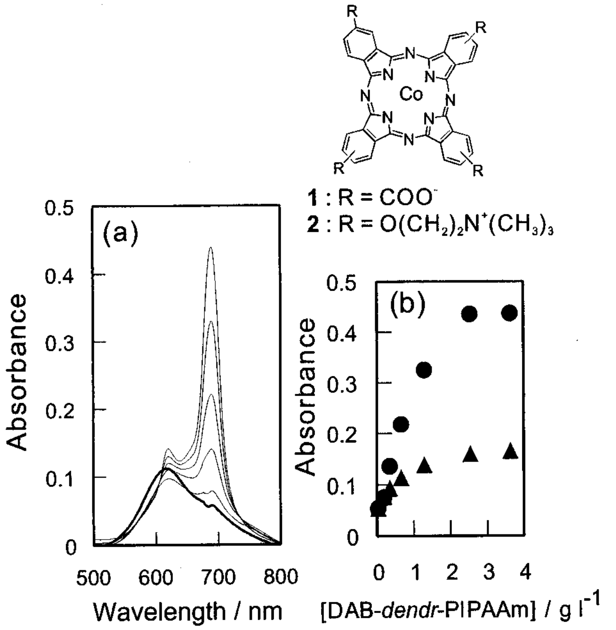

Figure 2. (a) Absorption spectra of **1** (4.66μM) in water in the presence of DAB-*dendr*-PIPAAm ([DAB-*dendr*-PIPAAm] = 0, 0.16, 0.31, 0.63, 1.25, 2.5 g/L). (b) Effect of DAB-*dendr*-PIPAAm concentration on absorbance at 688 nm of **1** (●) and **2** (▲) in water.

of four molecules of thiol is accompanied by that of one molecule of dioxygen:

$$4RSH + O_2 \xrightarrow{\text{catalyst}} 2RS{-}SR + 2H_2O$$

The catalytic activities of **1** for 2-mercaptoethanol (RSH) in water in the presence of DAB-*dendr*-PIPAAm and unmodified poly(propyleneimine) dendrimer are given in Table 1. The turnover frequency for **1** incorporated into DAB-*dendr*-PIPAAm (initial rate 82 turnovers per [**1**] per minute) is only 6% of that with the poly(propyleneimine) dendrimer at 25 °C. The difference in these reactivities implies that the penetration of the reacting molecules (RSH and dioxygen) is significantly restricted by PIPAAm arms. Figure 3 shows the temperature dependence of the initial rate (V_0) for the RSH oxidation catalyzed by **1** with DAB-*dendr*-PIPAAm. The V_0 value increases steeply and the turnover frequency is 3 times greater after the temperature was increased from 34 to 36 °C. This temperature is consistent with the LCST of PIPAAm arms as shown in the inset of Figure 3. We propose that this specific temperature dependence of the catalytic activity is induced by the structural changes in the dendritic host. Below LCST, the PIPAAm arms in DAB-*dendr*-PIPAAm are soluble and adopt an expanded conformation in water. The sterically crowed PIPAAm arms hinder substrate penetration. When the temperature of a solution is raised above LCST, the PIPAAm arms in DAB-*dendr*-PIPAAm will phase-separate and shrink. The incorporated catalyst is accessible to substrates after the PIPAAm arms shrink.

Table 1. Catalytic Activity of 1 in the Presence of DAB-*dendr*-PIPAAm and Poly(propyleneimine)dendrimer in Water[a]

host (concentration)	temp (°C)	initial reaction rate (turnovers per [**1**] per min)
DAB-*dendr*-PIPAAm	25	82
(2.90 g/L)	35	110
	36	337
poly(propylene imine)dendrimer	25	1368
(24.0 μM)	36	1621

[a] The turnover frequency was calculated from the initial dioxygen consumption rate (V_0). [**1**] = 1.90 μM; [O_2] = 0.24 mM; [RSH] = 10.0 mM.

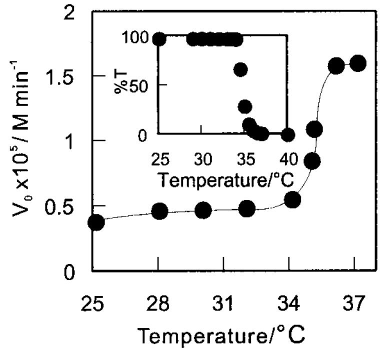

Figure 3. Temperature dependence of initial rate (V_0) in the presence of DAB-*dendr*-PIPAAm in aqueous solution at pH 6.80. [**1**] = 1.90μM, [O_2] = 0.24 mM, [RSH] = 10.0 mM, and [DAB-*dendr*-PIPAAm] = 2.90 g /L. Inset: Temperature dependence of transmittance for an aqueous solution of DAB-*dendr*-PIPAAm at 550 nm.

In summary, we prepared the dendrimer-based multiarm copolymer with PIPAAm arms that acts as a temperature-sensitive nanoscopic capsule for catalysts.

The catalytic activity is controlled in response to change in polymer conformations. These copolymers could in principle be applied to many "nanoscopic smart" materials including drug delivery, diagnostics, and separations by combining dendrimers with a variety of polymers.

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Supporting Information Available: Text giving experimental procedures and characterization of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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