Probe-Induced Self-Aggregation of γ-Cyclodextrin: Formation of Extended Nanotubular Suprastructure

ARTICLE *in* THE JOURNAL OF PHYSICAL CHEMISTRY C · JUNE 2008

Impact Factor: 4.77 · DOI: 10.1021/jp801951j

4 AUTHORS:

Paramita Das

27 PUBLICATIONS **746** CITATIONS

SEE PROFILE

Arabinda Mallick

Kashipur M. M. Mahavidyalaya

45 PUBLICATIONS **1,510** CITATIONS

SEE PROFILE

Deboleena Sarkar

Unilever

31 PUBLICATIONS **384** CITATIONS

SEE PROFILE

Nitin Chattopadhyay

Jadavpur University

134 PUBLICATIONS **2,873** CITATIONS

SEE PROFILE

Probe-Induced Self-Aggregation of γ-Cyclodextrin: Formation of Extended Nanotubular Suprastructure

Paramita Das, Arabinda Mallick,† Deboleena Sarkar, and Nitin Chattopadhyay*

Department of Chemistry, Jadavpur University, Calcutta 700 032, India

Received: January 22, 2008; Revised Manuscript Received: April 2, 2008

Time-resolved fluorescence anisotropy decay analysis, dynamic light scattering (DLS), and transmission electron microscopy (TEM) techniques have been exploited to substantiate and characterize the formation of a substrate-anchored γ-cyclodextrin nanotubular suprastructure in aqueous medium, the diameter and the length of the entity being ∼250 nm and a few micrometers, respectively. Similar aggregation is not observed with α- and β-cyclodextrins. Dimensions of the substrate and the cyclodextrin cavity have been ascribed to control the formation of the substrate-induced elongated aggregates. The report projects a simple way to design nanotubes of variable dimensions with a proper choice of the anchoring probe and the cyclodextrin.

1. Introduction

The design and preparation of supramolecular nanostructures is a challenging field with increasing attention because of their intrinsic scientific interest and technological applications in diverse fields such as a carrier for targeted drug or gene delivery, biochemical sensors, electronic or photonic material, and nanoreactors, etc. Self-assembly is a more friendly strategy for the preparation of the suprastructures compared to synthesizing them bond by bond. Spontaneous or induced self-assembly and chemical transformation of biological or organic subunits (molecules, macromolecules, and supramolecules) in a wide range of scientific fields are crucial subjects for the accomplishment of well-defined nanostructures and the precise control of the function of supramolecules at the molecular level.[1–11] In particular, vesicular and tubular assemblies are of much interest because of their unique characteristics as biomimetic systems. With potential applications across the food chain (in pesticides, vaccines, veterinary medicine, and nutritionally enhanced food), these nano- and microformulations are being developed day by day. Self-assembly of synthetic building blocks by noncovalent interactions is thus expected to provide a unique methodology for the development of supramolecular functional materials of the new generation.[1,2,4,10–14] The topic demands attention from medical research considering the prospective application of these nanostructures for selected and targeted drug delivery. Such an operation to the affected cell is always a challenging task to the present-day chemist and biologist because before doing that one has to ensure that the drug is well-protected during its transportation and delivery. Supramolecular assemblies can provide such opportunities to the drug molecules.[15,16]

Cyclodextrins (CDs) are interesting microvessels capable of embedding appropriately sized molecules, and the resulting supramolecules can serve as excellent miniature models for enzyme−substrate complexes. The cyclodextrin molecules have an internal cavity accessible to guest molecules of proper dimension through an opening of 4.5−5.3, 6.0−7.0, and 7.5−8.5 Å for α-CD, β-CD, and γ-CD, respectively.[5,6] The depths of all the CDs are more or less the same (7.9 Å). Depending on the relative dimensions of the guest molecule and the CD cavity together with the concentration of the CD, different host−guest stoichiometries are possible.[6,17,18] Cyclodextrin complexation can give beneficial modification of the guest molecules in terms of solubility enhancement, physical isolation of incompatible compounds, stabilization of labile guests, and control of their volatility for the long-term protection of color, odor, and flavor. The chemical reactivity of the guest can also be tuned by its incorporation into the cavity. Cyclodextrin nanocavity plays a key role in many biological processes to control the dynamics of a molecule confined in it.[6] Due to their great usefulness in the areas of synthetic, analytical, pharmaceutical, and biological chemistry, a number of studies have been undertaken to understand the nature of the complexes of CDs.

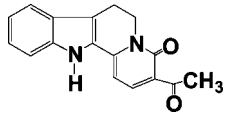
Cyclodextrins are known to self-aggregate through hydrogen bonding to form nanostructures. While α- and γ-CDs form only spherical aggregates in water medium, β-CD forms an elongated nanostructure.[19,20] This difference explains the relatively poor water solubility of β-CD compared to the other two.[19] Fluorescence anisotropy, transmission electron microscopy (TEM), NMR, scanning electron microscopy (SEM), dynamic light scattering (DLS), and X-ray diffraction are the general tools exploited to characterize the nanostructures. These studies illustrate the self-aggregation of cyclodextrins in aqueous solution, the extent of aggregation depending on the dimensions as well as the concentrations of cyclodextrins. González-Gaitano et al., using DLS technique, characterized polydisperse aggregates of unsubstituted CDs (α-, β-, and γ-CDs) in aqueous solution, where they reported the dimensions of the aggregates to be in the range of 200−300 nm.[20] Formation of supramolecular structures through the involvement of small molecules has been reported only recently.[15,16,21–35] Pistolis and Balomenou have shown that 2,5-diphenyl-1,3,4-oxadiazole (PPD) forms nanotubular suprastructure with γ-CD, contrary to the simple stoichiometric (1:1) complexes formed with α- and β-CDs.[15] The same school, in another study, reported the effect of the length of polyene series on the formation of nanotubes with γ-cyclodextrin.[23] They observed that the longest polyene within the studied series facilitates the formation of the longest tubular structures with γ-cyclodextrin. Using time-resolved fluorescence anisotropy technique, Roy et al. reported the formation of linear aggregates of γ-cyclodextrin anchored by coumarin 153.[24] DPH

* To whom correspondence should be addressed: Fax: 91-33-2414-6266. E-mail: nitin.chattopadhyay@yahoo.com.

† Present address: Division of Frontier Material Science, Graduate School of Engineering Science, Osaka University, Toyonaka 5608531, Japan.

10.1021/jp801951j CCC: $40.75
Published on Web 06/06/2008

SCHEME 1: Structure of AODIQ



(1, 6-diphenyl-1,3,5-hexatriene) induces γ-CD nanotube formation not only in aqueous solution but also in mixed solvents.[33] β-CD does not form such structure with DPH in mixed solvents, but it does in water.[33] All these current works establish that the cavity size of cyclodextrins controls the formation as well as the dimension of the probe−CD aggregates.[15,22–25,33] With these reports in hand the intention of our present work is to characterize the formation of fluorophore-anchored nanotubular linear aggregates and to find the role of the dimension of the CDs in this effect.

3-Acetyl-4-oxo-6,7-dihydro-12*H*-indolo-[2,3-*a*]quinolizine, AODIQ, a neutral molecule belonging to the group of the bioactive indole family, has recently been shown to be an excellent fluorescent probe for biological systems.[18,36–39] The indole nucleus renders a promising basis for the design and synthesis of new derivatives to protect the nervous system.[40] Considering the potential of the indole-based drug molecule in biophysical applications, we have, in this work, developed and characterized the AODIQ-anchored γ-cyclodextrin elongated nanotubular suprastructure. The impact of cyclodextrin cavity size in affecting the geometry of the resulting adducts has been recognized as the key factor for the formation of such elongated aggregates. We have exploited time-resolved fluorescence anisotropy, DLS, and TEM techniques for the purpose. To the best of our knowledge, this is the first report for the formation of a probe-anchored cyclodextrin-based elongated suprastructure using a biologically active *indole-based* drug molecule.

2. Experimental Section

3-Acetyl-4-oxo-6,7-dihydro-12H indolo-[2,3-a] quinolizine (Scheme 1) was synthesized in the laboratory using the method mentioned elsewhere.[39] It was purified by column chromatography, and the purity of the compound was checked by thin-layer chromatography (TLC). The compound was further vacuum-sublimed before use. α-Cyclodextrin, β-cyclodextrin, and γ-cyclodextrin (Fluka) were used as received without further purification. Triply distilled water was used for making the experimental solutions. Absorption and steady-state fluorescence measurements were performed using a Shimadzu MPS 2000 spectrophotometer and a Spex Fluorolog II spectrofluorimeter, respectively.

Fluorescence anisotropy decay [$r(t)$] measurements were performed in a time-correlated single photon counting spectrometer using nanoLED-07 (IBH, U.K.) as the light source at 408 nm. The typical response time of this system was 70 ps. Emissions at parallel ($I_{||}$) and perpendicular ($I_{\perp}$) polarizations were collected by rotating the analyzer at regular intervals. $r(t)$ was calculated using the following relation:

$$r(t) = [I_{||}(t) - GI_{\perp}(t)]/[I_{||}(t) + 2GI_{\perp}(t)] \quad (1)$$

where G is the correction factor for the detector sensitivity to the polarization detection of the emission.[38]

DLS measurements were performed in a Nano-ZS (Malvern) instrument (5 mW HeNe laser; $\lambda = 632$ nm) using DTS software. The sample was poured into a DTS0112 low volume disposal sizing cuvette of 1.5 mL (path length, 1 cm). The operating procedure was programmed in such a way that there were averages of 25 runs, each run being averaged for 15 s, and then a particular hydrodynamic diameter was evaluated using the DTS software.[41]

TEM measurement was performed using a JEOL, JEM 2010, transmission electron microscope operated at an accelerating voltage ranging from 100 to 200 kV. Samples for TEM were prepared by directly dropping the dispersion onto the carbon-coated copper grid followed by air-drying.

3. Results and Discussions

3.1. Steady-State Absorption and Emission. Steady-state absorption and fluorescence of AODIQ in aqueous and aqueous cyclodextrin environments are already discussed in one of our recent reports.[18] However, for an understanding of the perspective of the experiments reported herein to the general readership, we intend to highlight only the salient features of the steady-state results. The absorption spectrum of an aqueous solution of AODIQ shows a broad and unstructured low-energy band with a maximum at around 420 nm. Addition of CDs to the aqueous solution of AODIQ hardly changes the absorption spectra.

Room-temperature emission spectrum of AODIQ in aqueous medium is characterized by a broad unstructured band with maximum at around 520 nm ascribed to the ICT transition within the fluorophore.[42] Gradual addition of the CD to the aqueous solution of the probe leads to a hypsochromic shift of the emission maximum, an enhancement in the fluorescence yield, and a narrowing of the emission band. All these observations suggest that the polarity of the CD environment is less than the polarity of the bulk aqueous phase since similar effects have been observed in less polar solvents.[18,42,43] The increase in the fluorescence quantum yield in the CD environments was rationalized from the consideration of the relative stabilization of the ICT state of the probe.[18,43]

3.2. Time-Resolved Fluorescence Anisotropy. Our recent work on the photophysics of AODIQ in aqueous cyclodextrin environments reveals that a proper matching of the γ-CD cavity with the dimension of the probe leads to a remarkably higher steady-state fluorescence anisotropy compared to the probe−α-CD and probe−β-CD complexes. The steady-state anisotropy of AODIQ in water was found to be 0.04. In the CD environments the steady-state anisotropy increased gradually with an increase in the CD concentration leading to a saturation value (0.056 in α-CD, 0.059 in β-CD, and 0.142 in γ-CD).[18] Time-resolved fluorescence anisotropy of the probe is much more sensitive than the steady-state one, yielding structural and dynamical information about the fluorophore in an organized medium. Fluorescence anisotropy decay study is directly linked with the reorientational dynamics of the excited fluorophore and hence best suited for the investigation of molecular dynamics near the binding site and thereby for the structural information.[44,45] In the present study, time-dependent anisotropy decay experiments of the probe have been performed in aqueous and in different cyclodextrin environments. Figure 1 illustrates the fluorescence anisotropy decays of AODIQ in aqueous and different aqueous cyclodextrin environments. In pure aqueous medium the anisotropy decay is single-exponential. Figure 1 reveals that the decay pattern of the fluorophore in the presence of sufficiently high concentration of γ-CD differs remarkably from that in the other situations. In aqueous and in aqueous α-CD, β-CD, and lower concentration of γ-CD, the fluorescence anisotropy turns to zero within the fluorescence lifetime of the probe in the medium (∼1 ns). In the presence of sufficiently high concentration of γ-CD, however, the fluorophore exhibits biexponential anisotropy decay with a fast component and a *very long component* appearing to residual anisotropy in our monitoring time range, much longer than its fluorescence lifetime.[18,28,29]

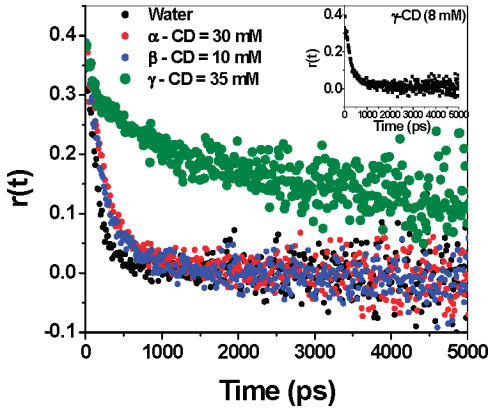


Figure 1. Fluorescence anisotropy decays of AODIQ in aqueous and aqueous cyclodextrin environments. Inset gives the decay of AODIQ in low concentration of γ-CD (8 mM).

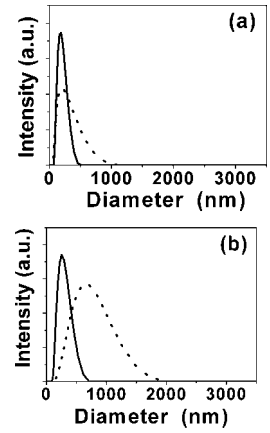


Figure 2. DLS results of the aqueous γ-CD solutions in the absence (—) and in the presence (•••) of AODIQ: (a) 8 and (b) 35 mM γ-CD.

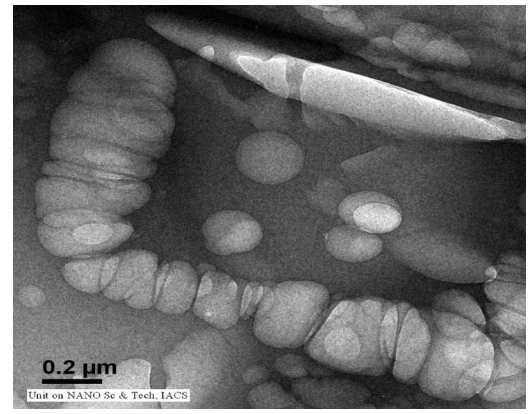


Figure 3. TEM image of elongated AODIQ-anchored γ-CD nanostructure.

In view of the contemporary interpretation of biexponential behavior in time-resolved anisotropy decay of a probe in the γ-cyclodextrin environment, it is necessary to address the issue of local (rotation of the probe within the aggregate) and/or global rotational dynamics (rotation of the whole aggregate).[46–48] At the high concentration of γ-CD, appearance of residual anisotropy in Figure 1 suggests that the hydrodynamic size of the host—guest complex is very large (considering the measured small difference in the fluorescence lifetime and assuming that the macroscopic viscosity does not differ very much in the different CD environments). The very large rotational time is ascribed to the tumbling motion of the AODIQ—γ-CD aggregate. In membrane or viscous environment (as in an ionic liquid or a gel network) appearance of such high residual anisotropy (restricted rotation) is well-known,[38] but in cyclodextrin environment such a high residual anisotropy is not well-documented in the literature. Recently, such an interesting observation was reported by Roy et al. when they were investigating the rotational and solvation dynamics of coumarin in cyclodextrin cavity.[24] They explained this issue grossly by invoking the formation of cyclodextrin nanotubular suprastructure. In a similar tune, our observation points to the formation of an elongated nanoaggregate in concentrated γ-CD solution. To characterize and obtain an approximate dimension of the AODIQ—γ-CD suprastructure, in the forthcoming sections, we have exploited dynamic light scattering and transmission electron microscopic techniques.

3.3. Dynamic Light Scattering Study. DLS measurement provides an effective way to investigate the macromolecular and supramolecular assemblies.[49,50] It estimates the diffusion coefficient from which the hydrodynamic radius of the particle (R_h) can be extracted using the Stokes—Einstein equation considering the assembly to be spherical.[51,52] Figure 2 projects the results obtained from the DLS study. It reveals single modal size distributions in aqueous solutions of 8 and 35 mM γ-CD in the absence of the probe molecule giving the hydrodynamic diameters (HD) of 200 and 250 nm, respectively, supporting the formation of the γ-CD aggregates.[20,25] Upon addition of the probe (AODIQ), in dilute solutions of γ-CD the DLS maximum remains undisturbed, showing only a widening of the distribution (Figure 2a). Interestingly, in the presence of 35 mM γ-CD the DLS study reflects a dramatic increase in the HD value, from 250 to 615 nm (Figure 2b).

Figure 2, thus, reveals that a high concentration of γ-CD results in the formation of a new structure other than the self-aggregated γ-CD. Arguing in the same line with some of the recent reports,[19–25,27] we propose that in the presence of AODIQ a probe-anchored nanotubular suprastructure is formed at high concentrations of γ-CD (Figure 2b).

3.4. Transmission Electron Microscopic Study. Since DLS gives only an average HD, to get direct evidence or an image of the nanoaggregate, we took TEM images of the γ-CD structures in the absence and in the presence of AODIQ. Consistent with the existing literature, the TEM picture of γ-CD aggregates in the absence of added AODIQ shows only globular structures with HD around 200—250 nm. In the presence of the anchoring probe, on the contrary, elongated nanostructures have been observed (Figure 3). Figure 3 shows that the diameter of the tubular/rodlike suprastructure remains in the same range while the length extends up to a few micrometers.

The dimension of the elongated AODIQ-anchored γ-CD nanostructure justifies the *very long* component of the aforesaid anisotropy decay. It is pertinent to emphasize that α-CD and β-CD do not form this type of AODIQ-induced extended suprastructure. A proper matching between the dimension of the probe and the γ-CD cavity size is ascribed to be responsible for the formation of the extended structure.[18,20–25] Taking, from the DLS study, the effective HD of AODIQ-anchored γ-CD suprastructure to be 600 nm for a hypothetical spherical shape, we calculate the length of the nanotube/rod to be around ~2.3 μm considering the diameter to be 250 nm as obtained from the DLS and TEM studies. This dimension is corroborated by the TEM picture (Figure 3).

It is important now to look into the basis of the formation of such a "nanotube" and the forces responsible for the formation of the aggregates. The role of the probe toward its anchoring action might be the result of an insubstantial equilibrium among

various forces favoring or disfavoring the process. There are effectively two forces that can contribute to the formation of the AODIQ−γ-CD complex. One is the van der Waals force of attraction between AODIQ and the interior of the CD cavity; the other is the H-bonding interaction between the ring OH groups of the cyclodextrin moieties. The latter is known to contribute toward self-association of the γ-CDs.[19–25,27,33] Since γ-CD forms a tubular structure only in the presence of the probe, van der Waals force of interaction seems to be important for the formation of the nanotube. Importance of H-bonding has been established looking at the event at a solution pH high enough to render hydrogen bonding ineffective.[27] For the purpose we carried out the steady-state anisotropy experiment under various pH conditions. It is observed that in sufficiently alkaline pH (≈12.0) the anisotropy value falls sharply, indicating the breakdown of the associated structure. This experiment unambiguously establishes the role of hydrogen bonding in the self-association process.[25,27,33] We, thus, conclude that both the van der Waals force of attraction and H-bonding play important roles during the formation of the nanotube. Since the extended suprastructure is not formed either in aqueous α- or β-CD, proper matching of the dimensions of the guest and the cavity of the CD appears responsible for the formation of such aggregates. Cyclodextrins, therefore, have a controlling role on the formation of the nanotubular supramolecular structures. The choice of probes of different dimensions and different cyclodextrins, thus, provides us a simple way to design the supramolecular nanostructure of desired dimension.

Conclusion

Time-resolved fluorescence anisotropy, DLS, and TEM studies reveal that interaction of the biologically active β-carboline derivative, AODIQ, forms nanotubular/rodlike elongated nanostructure with γ-CD at its high concentration. A proper matching of the dimensions of the fluorophore with the cyclodextrin cavities, van der Waals force of attraction, and hydrogen-bonding interaction have been argued to be responsible for the formation of the elongated supramolecular structure. The present article projects a simple way to design nanotubular suprastructures of desired dimensions through a proper choice of the anchoring probe and the cyclodextrin.

Acknowledgment. Financial support from DBT and CSIR, Government of India, are gratefully acknowledged. P.D. and D.S. thank CSIR for research fellowships. The authors greatly appreciate the cooperation received from Prof. N. Sarkar and Dr. A. Chakraborty of I.I.T., Kharagpur, and Prof. A. K. Dasgupta and Mr. J. Bhattacharya of Calcutta University for their kind help in time-resolved anisotropy and DLS measurements, respectively.

References and Notes

(1) Hill, J. P.; Jin, W.; Kosaka, A.; Fukushima, T.; Ichihara, H.; Shimomura, T.; Ito, K.; Hashizume, T.; Ishii, N.; Aida, T. *Science* **2004**, *304*, 1481.

(2) Fernandez-Lopez, S.; Kim, H. S.; Choi, E. C.; Delgado, M.; Granja, J. R.; Khasanov, A.; Kraehenbuehl, K.; Long, G.; Weinberger, D. A.; Wilcoxen, K. M.; Ghadiri, M. R. *Nature* **2001**, *412*, 452.

(3) Whitesides, G. M.; Grzybowski, B. *Science* **2002**, *295*, 2418.

(4) Shimizu, T.; Masuda, M.; Minamikawa, H. *Chem. Rev.* **2005**, *105*, 1401.

(5) Li, S.; Purdy, W. C. *Chem. Rev.* **1992**, *92*, 1457.

(6) Douhal, A *Chem. Rev.* **2004**, *104*, 1955.

(7) Vauthey, S.; Santoso, S.; Gong, H.; Watson, N.; Zhang, S. *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 5355.

(8) Ishii, D.; Kinbara, K.; Ishida, Y.; Ishii, N.; Okochi, M.; Yohda, M.; Aida, T. *Nature* **2003**, *423*, 628.

(9) Bong, D. T.; Clark, T. D.; Granja, J. R.; Ghadiri, M. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 988.

(10) Reches, M.; Gazit, E. *Science* **2003**, *300*, 625.

(11) Martin, C. R.; Kohli, P. *Nat. Rev. Drug Discovery* **2003**, *2*, 29.

(12) Guo, X.; Szoka, F. C., Jr *Acc. Chem. Res.* **2003**, *36*, 335.

(13) Percec, V.; Glodde, M.; Bera, T. K.; Miura, Y.; Shiyanovskaya, I.; Singer, K. D.; Balagurusamy, V. S. K.; Heiney, P. A.; Schnell, I.; Rapp, A.; Spiess, H.-W.; Hudson, S. D.; Duan, H. *Nature* **2002**, *417*, 384.

(14) Jang, W. D.; Jiang, D. L.; Aida, T. *J. Am. Chem. Soc.* **2000**, *122*, 3232.

(15) Pistolis, G.; Balomenou, I. *J. Phys. Chem. B* **2006**, *110*, 16428.

(16) Park, C.; Lee, I. H.; Lee, S.; Song, Y.; Rhue, M.; Kim, C. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 1199.

(17) Mallick, A.; Haldar, B.; Chattopadhyay, N. *J. Photochem. Photobiol. B: Biol.* **2005**, *78*, 215.

(18) Das, P.; Chakrabarty, A.; Haldar, B.; Mallick, A.; Chattopadhyay, N. *J. Phys. Chem. B* **2007**, *111*, 7401.

(19) Coleman, A. W.; Nicolis, I.; Keller, N.; Dalbiez, J. P. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1992**, *13*, 139.

(20) González-Gaitano, G.; Rodríguez, P.; Isasi, J. R.; Fuentes, M.; Tardajos, G.; Sánchez, M. *J. Inclusion Phenom. Mol. Reconnit. Chem.* **2002**, *44*, 101.

(21) Li, G.; McGown, L. B. *Science* **1994**, *264*, 249.

(22) Harada, A.; Li, J.; Kamachi, M. *Nature* **1993**, *364*, 516.

(23) Pistolis, G.; Malliaris, A *J. Phys. Chem. B* **1998**, *102*, 1095.

(24) Roy, D.; Mondal, S. K.; Sahu, K.; Ghosh, S.; Sen, P.; Bhattacharyya, K. *J. Phys. Chem. A* **2005**, *109*, 9716.

(25) Wu, A.; Shen, X.; He, Y. *J. Colloid Interface Sci.* **2006**, *302*, 87.

(26) Cheng, X.; Wu, A.; Shen, X.; He, Y. *Acta Phys.-Chim. Sin.* **2006**, *22*, 1466.

(27) He, Y.; Fu, P.; Shen, X.; Gao, H. *Micron*, in press.

(28) Zhang, C.; Shen, X.; Gao, H. *Chem. Phys. Lett.* **2002**, *363*, 515.

(29) Wu, A.; Shen, X.; He, Y. *J. Colloid Interface Sci.* **2006**, *297*, 525.

(30) Miyake, K.; Yasuda, S.; Harada, A.; Sumaoka, J.; Komiyama, M.; Shigekawa, H. *J. Am. Chem. Soc.* **2003**, *125*, 5080.

(31) Harada, A.; Li, A.; Kamachi, M. *Nature* **1992**, *356*, 325.

(32) Hernández-Pascacio, J.; Garza, C.; Banquv, X.; Dı´az-Vergara, N.; Amigo, A.; Ramos, S.; Castillo, R.; Costas, M.; Pineiro, A. *J. Phys. Chem. B* **2007**, *111*, 12625.

(33) Pistolis, G.; Malliaris, A. *J. Phys. Chem.* **1996**, *100*, 15562.

(34) Wen, X. H.; Liu, M.; Tan, F. *Chem. Lett.* **2004**, *33*, 894.

(35) (a) Mallick, A.; Mandal, M. C.; Haldar, B.; Chakrabarty, A.; Das, P.; Chattopadhyay, N. *J. Am. Chem. Soc.* **2006**, *128*, 3126. (b) Mallick, A.; Mandal, M. C.; Haldar, B.; Chakrabarty, A.; Das, P.; Chattopadhyay, N. *J. Am. Chem. Soc.* **2006**, *128*, 10629.

(36) Mallick, A.; Haldar, B.; Chattopadhyay, N. *J. Phys. Chem. B.* **2005**, *109*, 14683.

(37) Mallick, A.; Haldar, B.; Maiti, S.; Bera, S. C.; Chattopadhyay, N. *J. Phys. Chem. B* **2005**, *109*, 14675.

(38) Lakowicz, J. R. *Principles of Fluorescence Spectroscopy*; Springer: New York, 2006.

(39) Giri, V. S.; Maiti, B. C.; Pakrashi, S. C. *Heterocycles* **1984**, *22*, 233.

(40) Stolc, S. *Life Sci.* **1999**, *65*, 1943.

(41) Bhattacharya, J.; Jasrapuria, S.; Sarkar, T.; GhoshMoulick, R.; Dasgupta, A. K. *Nanomedicine* **2007**, *3*, 14.

(42) Mallick, A.; Maiti, S.; Haldar, B.; Purkayastha, P.; Chattopadhyay, N. *Chem. Phys. Lett.* **2003**, *371*, 688.

(43) Mallick, A.; Haldar, B.; Maiti, S.; Chattopadhyay, N *J. Colloid Interface Sci.* **2004**, *278*, 215.

(44) Das, P.; Mallick, A.; Chakrabarty, A.; Haldar, B.; Chattopadhyay, N. *J. Chem. Phys.* **2006**, *125*, 044516.

(45) Maiti, N. C.; Krishna, M. M. G.; Britto, P. J.; Periasamy, N. J. *J. Phys. Chem. B* **1997**, *101*, 11051.

(46) Balabai, N.; Linton, B.; Napper, A.; Priyadarshi, S.; Sukharevsky, A. P.; Waldek, D. H. *J. Phys. Chem. B* **1998**, *102*, 9617.

(47) El-Kemary, M.; Organero, J.; Santos, A. L.; Douhal, A. *J. Phys. Chem. B* **2006**, *110*, 14128.

(48) Tormo, L.; Organero, J. A.; Douhal, A. *J. Phys. Chem. B* **2005**, *109*, 17848.

(49) Feitosa, E.; Brown, W.; Wang, K.; Barreleiro, P. C. A. *Macromolecules* **2002**, *35*, 201.

(50) Almgren, M.; Gimel, J. C.; Wang, K.; Karlsson, G.; Edward, K.; Brown, W. *J. Colloid Interface Sci.* **1998**, *202*, 222.

(51) Robert, P. *Dynamic Light Scattering: Applications of Photon Correlation Spectroscopy*; Plenum: New York, 1985.

(52) Brown, W. *Light Scattering*; Oxford University Press, Oxford, U.K., 1996.

JP801951J