Phase Transfer of Hydrophilic, Cyclodextrin-Modified Gold Nanoparticles to Chloroform Solutions

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Abstract: The preparation and characterization of gold nanoparticles (~3 nm in diameter) capped with thiolated α- and β-cyclodextrins (α and β-CD) is described. The CD-capped nanoparticles are hydrophilic and bind ferrocene derivatives as evidenced by electrochemical and ^{1}H NMR spectroscopic measurements. The binding interactions of the CD-capped nanoparticles with a series of five alkyldimethyl(ferrocenylmethyl)ammonium ions (the alkyl group is propyl for compound **1**, heptyl for **2**, dodecyl for **3**, hexadecyl for **4**, and docosyl for **5**) can be utilized for the phase transfer of the hydrophilic, CD-capped nanoparticles into a nonpolar chloroform phase. Only **3**, **4**, and **5** act as effective phase transfer agents, since **1** and **2** do not have enough amphiphilic character. The structure of the aggregates formed upon transfer of the CD-capped nanoparticles to the chloroform solution is postulated to resemble that of reverse micelles, as the nanoparticles template the peripheral arrangement of the cationic ferrocene amphiphiles, counterions and water molecules around their surfaces.

Introduction

The fast development of methods for the preparation of metal and semiconductor nanoparticles capped with organic monolayers is opening interesting possibilities for the functionalization of their surfaces.[1] Among these, the attachment of functional groups capable of engaging in well-defined host−guest interactions is receiving considerable attention. For instance, Mirkin and co-workers have derivatized gold colloidal particles with oligonucleotides and used their recognition properties to form nanoparticle assemblies, as well as for the detection of specific nucleotide sequences.[2] The group of Fitzmaurice has done extensive work on the surface modification of titanium oxide and gold and silver nanoparticles with functional groups capable of hydrogen bonding interactions with solution species.[3] Rotello and co-workers have also derivatized gold nanoparticles with functional subunits that can interact via hydrogen bonding with partners in the solution.[4] Our group has focused on the modification of gold,[5] platinum,[6] and palladium[6] nanoparticles with thiolated cyclodextrins with the primary goal of using their well-documented host properties[7] to endow the nanoparticles with desirable features. In general terms, we would like to achieve nanocomposite systems (metal core/capping organic monolayer) that combine the best features of two worlds: the electronic, magnetic, and/or catalytic properties of the metal cores with the molecular recognition ability of the protecting organic monolayers.

Ferrocene derivatives have long been recognized as excellent guests for the cyclodextrins (CDs) in aqueous media.[8] In this work, we report on the binding interactions of gold nanoparticles capped with thiolated α-CD and β-CD hosts with a series of five cationic ferrocene derivatives (compounds **1**−**5**, see Scheme 1). More specifically, we focus on how these interactions can be utilized to transfer the hydrophilic CD-modified nanoparticles into low polarity solution phases. In fact, the CD-capped gold nanoparticles behave as seeds or templates for the formation of a novel type of aggregates that have a strong resemblance to reverse micelles.

Experimental Section

Materials. Hydrogen tetrachloroaurate(III) trihydrate, *N*,*N*′-dimethylformamide, ethanol, 1-adamantanol, and ferrocenemethanol were purchased from Aldrich and used without further purification. D_2O and $CDCl_3$ were supplied by Cambridge Isotope Laboratories and used as received. α-CD and β-CD were purchased from Cerestar and used

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[1] See, for instance: Templeton, A. C.; Wuelfing, W. P.; Murray, R. C. *Acc. Chem. Res*. **2000**, *33*, 27.

[2] (a) Mucic, R. C.; Storhoff, J. J.; Mirkin, C. A.; Letsinger, R. L. *J. Am. Chem. Soc.* **1998**, *120*, 12674. (b) Reynolds, R. A.; Mirkin, C. A.; Letsinger, R. L. *J. Am. Chem. Soc.* **2000**, *122*, 3795. (c) Storhoff, J. J.; Lazarides, A. A.; Mucic, R. C.; Mirkin, C. A.; Letsinger, R. L.; Schatz, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4640. (d) Taton, T. A.; Mucic, R. C.; Mirkin, C. A.; Letsinger, R. L. *J. Am. Chem. Soc.* **2000**, *122*, 6305. (e) Taton, T. A.; Mirkin, C. A.; Letsinger, R. L. *Science* **2000**, *289*, 1757.

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[4] (a) Boal, A. K.; Rotello, V. M. *J. Am. Chem. Soc.* **1999**, *121*, 4914. (b) Boal, A. K.; Ilhan, F.; DeRouchey, J. E.; Thurn-Albrecht, T.; Russell, T. P.; Rotello, V. M. *Nature* **2000**, *404*, 746.

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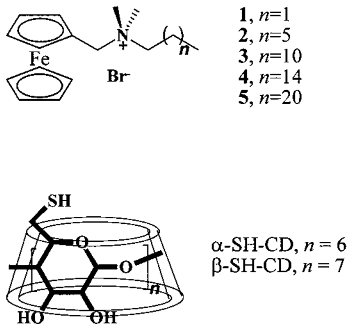
Scheme 1. Structures of the Compounds Used in This Work



without further purification. The thiolated cyclodextrins (see structures in Scheme 1) were synthesized as previously reported.[9] Ferrocene derivatives **1**−**5** (Scheme 1) were prepared by procedures similar to those reported by our group.[8f] All the compounds prepared for this work were fully characterized by NMR spectroscopy and FAB MS. House deionized water (∼10 MΩ·cm) was further purified to a minimum final resistivity of 18.1 MΩ·cm by passage through a four-cartridge Barnstead Nanopure II system. Thin-layer chromatography (TLC) was carried out with silica gel F-254 (Scientific Adsorbents).

UV−Vis Spectroscopic Measurements. Electronic absorption spectra were recorded with a Shimadzu UV-2101PC scanning spectrophotometer at 20 °C. Phase transfer of the CD-capped nanoparticles from aqueous into organic solutions was monitored by measuring the absorbance of the organic phase at 600 nm. The ferrocene derivatives do not absorb at this wavelength.

^{1}H NMR Measurements. ^{1}H NMR spectra (400 MHz) were recorded with a Varian VXR 400 spectrometer. In the complexation studies, the chemical shifts of the protons on the ferrocene derivatives were measured taking as the reference the residual HDO peak from the aqueous solvent system.

Transmission Electron Microscopic (TEM) Measurements. TEM images were obtained with a top-entry Philips EM 300 microscope. For a typical measurement, a single drop of gold nanoparticle solution was deposited with a pipet onto a carbon-coated copper grid and allowed to dry under ambient atmosphere for 5 min. Phase contrast images were recorded at an accelerating voltage of either 80 or 100 keV, and the resulting micrographs were obtained at magnifications of 163 000× and 185 800×. The size distribution of the modified gold nanoparticles was determined by measuring the diameters of at least 200 individual particles located in representative regions of the micrographs.

Electrochemical Measurements. Square wave voltammograms (SWV) of solutions containing the ferrocene derivatives in the absence and in the presence of surface-modified gold nanoparticles were recorded with a BAS 100 B/W electrochemical analyzer. The experiments were done in a single-compartment glass cell fitted with a glassy carbon working electrode (0.018 cm^2), a Pt flag auxiliary electrode, and a Ag/AgCl reference electrode. The parameters used to generate the excitation function for SWV measurements were as follows: step size, 4 mV; pulse amplitude, 25 mV; frequency, 15 Hz. All experiments were carried out in aqueous solution containing 0.1 M NaCl as the supporting electrolyte. The solutions were deoxygenated and maintained under nitrogen gas throughout the measurements.

Photon Correlation Spectroscopic (PCS) Experiments. A Coulter N4-Plus instrument was utilized to measure the sizes of the modified gold nanoparticles by PCS. All experiments were done at controlled temperature (20 °C). The scattered light was detected at 90° from the incident beam. The viscosity and refractive index of the gold nanoparticle solutions were taken as identical to the values of the corresponding pure solvents (water or chloroform).

Preparation of CD-Capped Gold Nanoparticles. We used a procedure similar to that previously reported by us.[5b] Briefly, equal volumes (20 mL) of $HAuCl_4$ (50 mg) in DMF and a second DMF solution containing $NaBH_4$ (75.5 mg) and β-SH-CD (32.5 mg) were quickly mixed. The reaction mixture developed a deep brown color immediately, but we allowed the reaction to proceed for 24 h with continuous stirring. At this point, a precipitate was collected by centrifugation and washed with DMF (4 × 50 mL) to remove free thiolated CD. The complete removal of this compound was verified by TLC. The solid product was further washed (4 × 50 mL) with ethanol/water (90:10 v/v), collected by centrifugation, and dried at 60 °C under vacuum for 24 h.

Determination of CD Surface Coverage. A carefully weighed sample (∼100 mg) of CD-capped gold nanoparticles was treated with 25 mL of acid solution (0.2 M HNO_3 + 0.2 M HCl) to redissolve the gold nanoparticles. The resulting solution was neutralized with 1.0 M NaOH, the solvent was evaporated, and the solid residue was dried overnight at 60 °C under vacuum. The dried residue was dissolved in 1 mL of DMSO-d_6 also containing a small amount of DMF as an internal standard and submitted to ^{1}H NMR analysis. The resulting spectrum was dominated by the spectral pattern corresponding to β-SH-CD, confirming that this compound is not degraded by the acidic conditions used to destroy the gold nanoparticles. The relative integral of the peak corresponding to H-1 of β-SH-CD versus the methyl resonance of DMF was compared to that obtained with a separate sample prepared by dissolving a known amount of free β-SH-CD in the same solvent system (DMSO-d_6 spiked with DMF). From this comparison, the absolute amount of β-SH-CD recovered from the capped nanoparticle sample could be determined, which allowed the determination of the CD surface coverage, since the diameter of the nanoparticles and, thus, their total exposed surface area were known from TEM measurements.

Results and Discussion

Preparation and Characterization of the Modified Gold Nanoparticles. The CD-capped nanoparticles used in this work were prepared by reduction of $AuCl_4^-$ in DMF solution also containing the thiolated CD host (α-SH-CD or β-SH-CD). The choice of solvent is dictated by the solubility of the thiolated CD hosts, which is very limited in many common organic solvents. As observed with other thiolated capping agents,[1] the [thiol]/[Au] ratio in the reaction mixture determines the average size of the resulting nanoparticles. Increasing the [thiol]/[Au] ratio leads to the production of smaller particles. Furthermore, at identical concentration levels, β-SH-CD yields smaller particles than α-SH-CD as a reflection of the larger number of thiol units in the former host. For instance, a 5:1 [Au]/[β-SH-CD] ratio yields nanoparticles with an average diameter of 2.9 ± 0.7 nm. To obtain similarly sized nanoparticles (diameter = 3.1 ± 0.7 nm) capped with α-SH-CD, we had to use a lower [Au]/[CD] ratio of 4:1. Figure 1 shows representative TEM images of both preparations. This figure also illustrates that the size distributions of these nanoparticle preparations are fairly narrow.

Figure 2 shows the ^{1}H NMR spectra (400 MHz, D_2O) of the CD-modified nanoparticles. The observed resonances appear at chemical shifts that correspond to those of the proton signals of the parent CDs. Remarkably, the signals for the nanoparticle-immobilized CDs are substantially broadened. This type of signal broadening has been observed by Murray and co-workers in alkanethiolate-capped gold clusters.[10] In these systems, the resonances of those protons closer to the metal surface are more seriously broadened, while the effect is less pronounced for the protons that are further away. Fast relaxation and environmental heterogeneities are thought to be responsible for these line broadening effects. In any instance, the NMR spectra of Figure 2 constitute clear evidence for the attachment of the thiolated CDs to the surface of the gold nanoparticles.

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[9] Rojas, M. T.; Königer, R.; Stoddart, J. F.; Kaifer, A. E. *J. Am. Chem. Soc.* **1995**, *117*, 336.

[10] Hostetler, M. J.; Wingate, J. E.; Zhong, C. J.; Harris, J. E.; Vachet, R. W.; Clark, M. R.; Londono, J. D.; Green, S. J.; Stokes, J. J.; Wignall, G. D.; Glish, G. L.; Porter, M. D.; Evans, N. D.; Murray, R. W. *Langmuir* **1998**, *14*, 17.

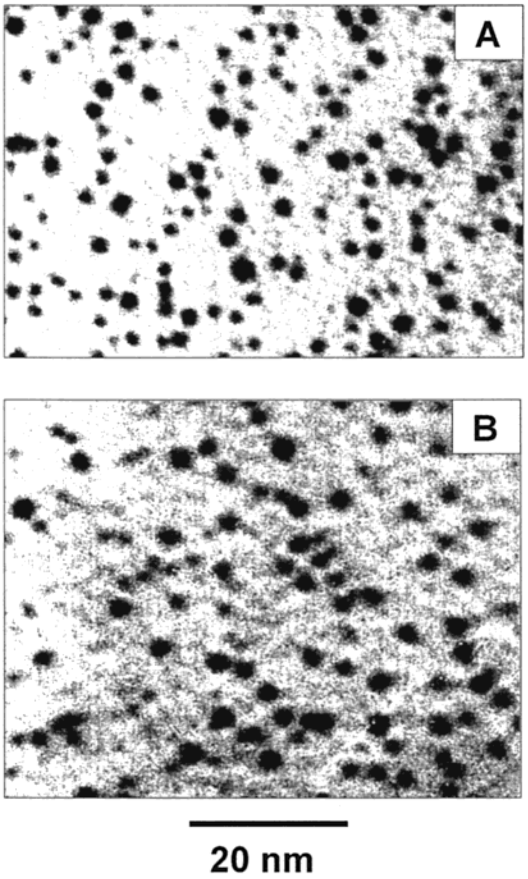

Figure 1. TEM images of (A) β-SH-CD-modified and (B) α-SH-CD-modified gold nanoparticles.

We have also recorded the FT-IR spectra of the modified gold nanoparticles. The spectra are similar (data not shown) to those reported before,[5a] corresponding to larger gold particles (13-nm diameter) derivatized with β-SH-CD. The spectral features are essentially identical with those recorded with the free CDs. The only noticeable difference is the disappearance of the S−H stretch at ~2300 cm^{-1} in the spectra of the modified nanoparticles, as anticipated due to the mode of attachment of the CDs to the gold surface. The surface plasmon resonance absorption of the nanoparticles is visible in their electronic absorption spectra (see Supporting Information), although relatively weak due to their small diameter, in good agreement with previous results.[5b]

An important point that we must address in these systems is the extent of CD surface coverage of the gold nanoparticles. We used a simple method (see Experimental Section) based on the redissolution of CD-capped gold nanoparticles of known diameter and the recovery and ^{1}H NMR quantitation of the β-SH-CD present in the sample to determine the fraction of nanoparticle surface covered by the CD hosts. It was assumed that an individual β-SH-CD host occupies an area[9] of 180 Å^2 and that the nanoparticles are perfect spheres so that their individual surface areas can be determined from their radius (r) as $4\pi r^2$. Repeated measurements with β-SH-CD-capped gold nanoparticles (diameter: 2.9 nm) gave a value of 75 ± 9% for the CD surface coverage. This means that the average particle is covered by ~10 covalently attached β-SH-CD hosts.

The excellent aqueous solubility of these CD-capped gold nanoparticles is an interesting result because of the relative scarcity of reported examples of water-soluble, thiol-derivatized gold particles in this size range.[11] The solubility properties are probably determined by the polarity of the secondary hydroxyl groups of the CD receptors, which afford a polar character to the surface of the nanoparticles. Surface attachment of the CD hosts through their primary faces necessarily leaves the wider, secondary faces exposed to the solution phase, a configuration that favors binding between the immobilized CDs and appropriate guests in the solution.

Binding of Ferrocene Derivatives to the Nanoparticle-Immobilized CD Hosts. While the formation of inclusion complexes between ferrocene derivatives and CD hosts is certainly well established in the literature,[8] we decided to verify that the CD hosts immobilized on the gold nanoparticles retain their binding ability. A few years ago our group demonstrated that β-SH-CD receptors immobilized onto gold electrodes maintained their host binding ability toward ferrocene guests in the contacting solution.[9] More recently, we have reported data that support the binding activity toward ferrocene dimers of β-SH-CD attached to the surface of larger (13 nm diameter) gold colloidal particles.[5a] In addition to this, clear electrochemical evidence for the complexation of ferrocenemethanol by gold nanoparticles (~3 nm diameter) capped with β-SH-CD has been obtained in our laboratory.[5b] We have also investigated the binding interactions between **1** and β-SH-CD-capped nanoparticles and found similar electrochemical data (see Supporting Information), which constitutes clear evidence for the binding of **1** to the nanoparticle-immobilized CD cavities.

The host−guest complexation phenomena between **1** and β-SH-CD-capped nanoparticles were further investigated by ^{1}H NMR spectroscopy. Figure 3 shows the spectral region corresponding to the ferrocene protons of **1** and the effects observed upon addition of CD-capped gold nanoparticles. Clearly, the presence of the nanoparticles leads to the displacement and broadening of the ferrocene proton resonances. The chemical shift displacements are attributed to the formation of the inclusion complexes on the nanoparticle surfaces, as they are similar to those observed upon the addition of free β-CD to solutions of ferrocene derivatives.[8f] The substantial line broadening must result also from the association of the ferrocene guest to the massive nanoparticles,[3e] and is probably related to chemical exchange (free ferrocene going to bound ferrocene and back), as well as to relaxation effects in the bound state. Note that when the ferrocene guest is bound to a CD cavity, it becomes a part of a rather large supramolecular assembly. Figure 4 shows the chemical shifts for two different protons in **1** as a function of the added concentration of β-SH-CD-capped nanoparticles. The proton on the ferrocene residue (open circles) exhibits clear complexation-induced shifts ($\Delta\delta$), which reach values larger than 0.1 ppm. On the other hand, the terminal methyl protons on the propyl chain of **1** exhibit very small $\Delta\delta$ values, strongly suggesting that the ferrocenyl group is the active site for complexation inside the CD cavity. Finally, addition of a competing guest to the solution (1-adamantanol) releases the ferrocene guests from their bound states in the nanoparticle CD cavities and the chemical shifts return to values close to those observed before the addition of the nanoparticles. A ^{1}H NMR spectroscopic study of the complexation of **1** by free β-CD yields similar results. All these spectroscopic data add further support to the formation of inclusion complexes between **1** and the particle-immobilized CD hosts. The combination of the NMR and electrochemical data presented here indicate that the

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[11] See, for instance: (a) Templeton, A. C.; Chen, S.; Gross, S. M.; Murray, R. W. *Langmuir* **1999**, *15*, 66. (b) Chen, S.; Kimura, K. *Langmuir* **1999**, *15*, 1075.

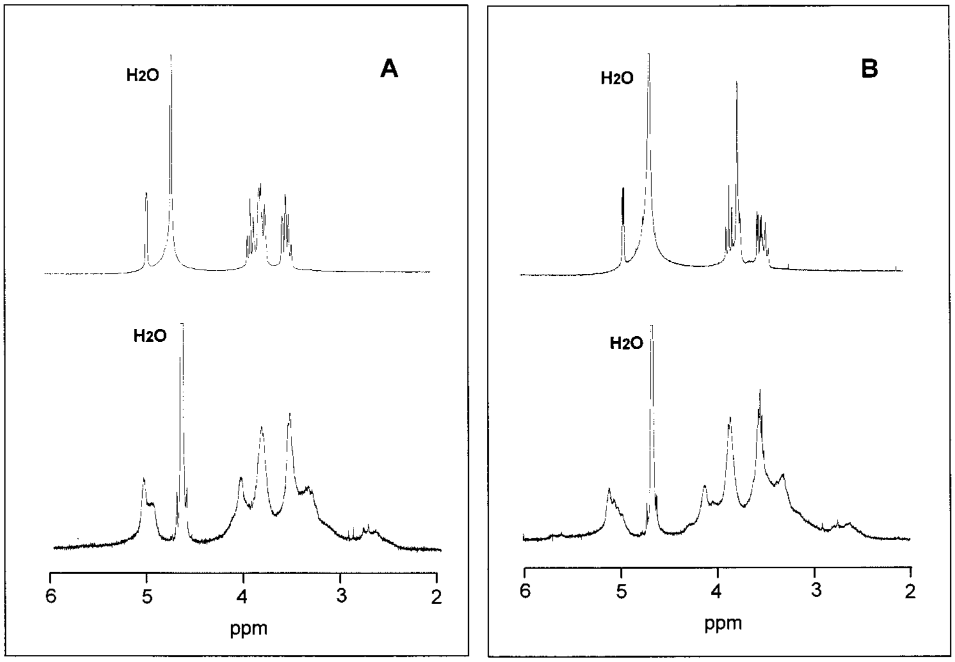

Figure 2. ^{1}H NMR spectra (D_2O) of (A) free α-CD (top) and α-CD immobilized on gold nanoparticles (bottom)and (B) free β-CD (top) and β-CD immobilized on gold nanoparticles (bottom).

CDs chemisorbed on the gold nanoparticles are effective hosts for binding of suitable guests in the solution.

Phase Transfer of CD-Capped Gold Nanoparticles into Organic Solutions. The noncovalent modification of macromolecules, such as DNA,[12] dendrimers,[13] and core−shell polymers,[14] is very relevant for the development of new materials with biomedical applications or altered solubility, as well as in coating formulations. Modification typically takes advantage of electrostatic interactions between charges on the surface of the macromolecules and the polar headgroups of surfactants. We reasoned that the host−guest interactions at the nanoparticle−solution interface investigated in this work could be used for similar purposes. Therefore, we prepared a series of analogues of compound **1** having longer aliphatic chains. Ferrocene derivatives **4** and **5** have well-defined amphiphilic character,[8f,15] while **2** and **3** have intermediate properties owing to their shorter chains. Thus, compounds **1**−**5** all have a ferrocene residue as well as a varying degree of amphiphilic character that increases from **1** to **5**. Correspondingly, their aqueous solubility decreases from **1** to **5**.

The CD-modified gold nanoparticles prepared in this work are very soluble in aqueous media, where they remain in solution without undergoing aggregation or flocculation for months. Our PCS measurements demonstrate that no aggregates are formed in solution over long periods of time. When an aqueous solution containing β-SH-CD-capped nanoparticles (1 mg/mL) is equilibrated with a chloroform solution of **5** (1 mM), the organic phase quickly becomes colored, drawing from the original deep brown color of the aqueous nanoparticle solution. Figure 5 shows the electronic absorption spectrum of the chloroform solution before and after equilibration with the nanoparticles. Before equilibration (Figure 5A), the only absorption band observed in the wavelength range surveyed corresponds to the ferrocene residue of **5** and has a λ_{max} of 430 nm. No absorption is observed at wavelengths longer than 550 nm. After equilibration with the nanoparticle solution, the spectrum is completely different, showing the characteristic absorption envelope of the nanoparticles and two peaks (λ_{max} at ∼430 and ∼510 nm) corresponding to absorptions by the ferrocene residues (compound **5**) and the nanoparticles (surface plasmon resonance band), respectively. Subtraction of the spectrum in Figure 5A from the spectrum in Figure 5B yields a spectrum characteristic of the nanoparticles (see Supporting Information). The obvious conclusion from these results is that compound **5** acts as an efficient phase transfer agent for the water-soluble, CD-capped gold nanoparticles and allows their solubilization in the chloroform phase. Since the ferrocene derivatives **1**−**5** do not exhibit electronic absorptions at 600 nm, we can use the absorbance at this wavelength to monitor the extent of nanoparticle phase transfer.

Is **5** an efficient phase transfer agent because of the long aliphatic chain in its structure? To address this question we investigated the remaining ferrocene derivatives under similar conditions. The results (see Figure 6) unequivocally demonstrate that the amphiphilic character afforded by the aliphatic chain is crucial to accomplish phase transfer of the nanoparticles. Thus, compounds **3**, **4**, and **5** (with aliphatic chains of 12, 16 and 22 carbon atoms) effectively promote the solubilization of the β-SH-CD-capped gold nanoparticles in the chloroform phase. By contrast, compounds **1** and **2** (with shorter aliphatic chains of 3 and 7 carbon atoms) are completely ineffective. The "threshold length" seems to be around 10 carbon atoms, although we have not determined this value in a very accurate fashion. Clearly, nanoparticle solubilization by compounds **1** to **5** in $CHCl_3$ is determined by the length of their aliphatic chain. This finding strongly suggests that the aliphatic chains arrange themselves on the periphery of the aggregates formed during these phase transfer phenomena.

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[12] (a) Sergeyev, V. G.; Mikhailenko, S. V.; Pyshkina, O. A.; Yaminsky, I. V.; Yoshikawa, K. *J. Am. Chem. Soc.* **1999**, *121*, 1780. (b) Mel'nikov, S. M.; Lindman, B *Langmuir* **1999**, *15*, 1923.

[13] Chechik, V.; Zhao, M. Q.; Crooks, R. M. *J. Am. Chem. Soc.* **1999**, *121*, 4910.

[14] (a) Sunder, A.; Kramer, M.; Hanselmann, R.; Mulhaupt, R.; Frey, H. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 3552. (b) Bakeev, K. N.; Shu, Y. M.; Zezin, A. B.; Kabanov, V. A. *Macromolecules* **1996**, *29*, 1320.

[15] The amphiphilic character of similar cationic ferrocene derivatives is well documented. See, for instance: (a) Saji, T.; Hoshino, K.; Aoyagui, S. *J. Am. Chem. Soc.* **1985**, *107*, 6865. (b) Donohue, J. J.; Buttry, D. A. *Langmuir* **1989**, *5*, 671.

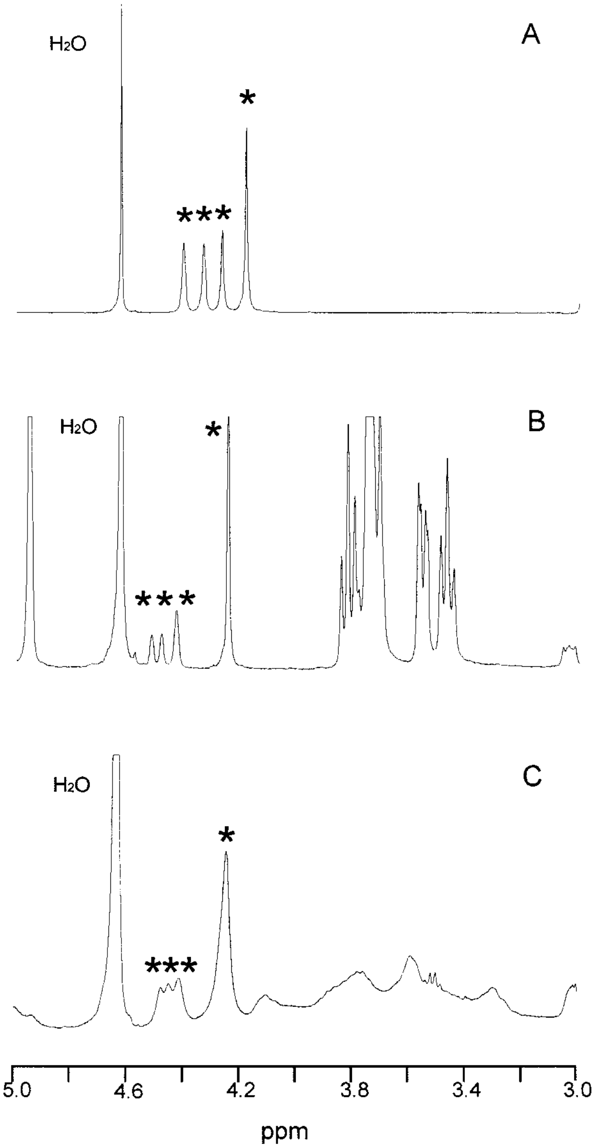


Figure 3. ^{1}H NMR spectra (400 MHz, D_2O) of (A) free **1** (2 mM), (B) **1** in the presence of 6 mM of β-SH−CD, and (C) **1** in the presence of 10 mg/mL of β-SH-CD-capped gold nanoparticles. The signals labeled with an asterisk correspond to the protons in the ferrocene moiety of compound **1**.

We also investigated phase transfer of nanoparticles as a function of the concentrations of amphiphilic ferrocene derivative and modified gold nanoparticles. Typical data for compound **3** and β-SH-CD-capped nanoparticles are shown in the Supporting Information. We observed that the concentration of nanoparticles transferred to the organic phase (as measured by their absorbance at 600 nm) increases with the initial concentration of **3** in the $CHCl_3$ phase while the initial concentration of nanoparticles in the aqueous phase was maintained at a fixed value (1.0 mg/mL). Conversely, the concentration of transferred nanoparticles also correlates with its initial concentration in the aqueous phase (0.1−0.5 mg/mL) when the concentration of compound **3** in the receiving phase is kept constant. These data are consistent with a transfer mechanism that involves the formation of interfacial complexes between the CD hosts on the nanoparticles and the ferrocene residues of the amphiphilic guests.

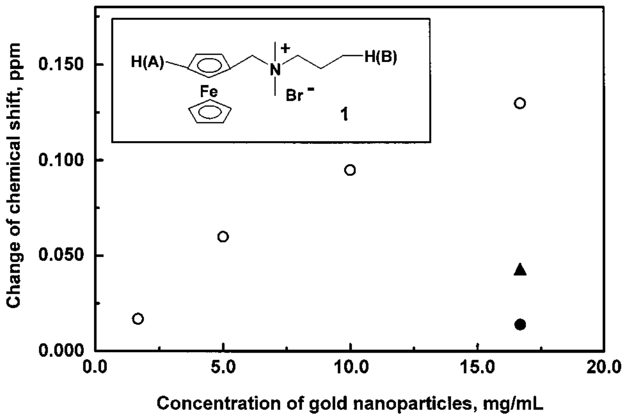


Figure 4. Effects on the chemical shifts of two protons in compound **1** (2 mM in D_2O) observed upon addition of β-SH-CD-capped gold nanoparticles at room temperature. (○) Proton A on ferrocene moiety. (●) Proton B on terminal methyl group. (▲) Proton A on ferrocene moiety after adding 4 mM 1-adamantanol.

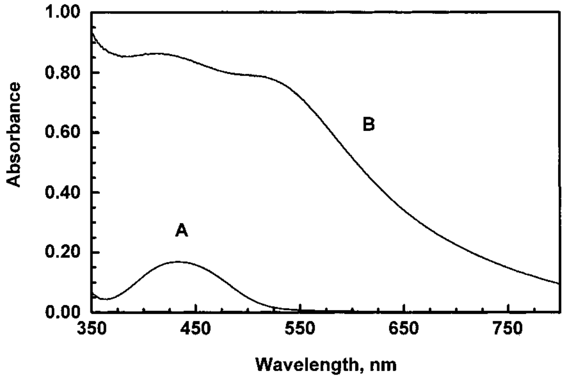


Figure 5. Visible spectrum of the chloroform phase containing 1 mM **5** (A) before equilibration and (B) after equilibration with an aqueous solution containing 1 mg/mL β-SH-CD-capped gold nanoparticles at 20 °C.

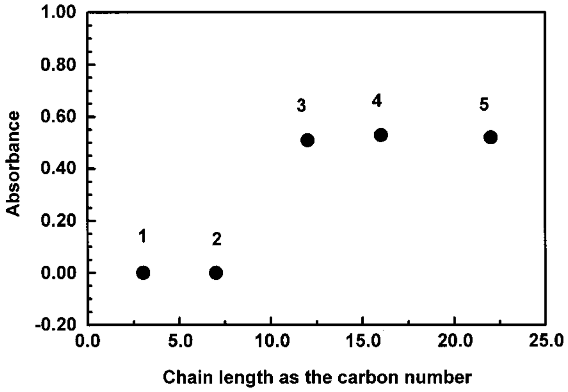


Figure 6. Absorbance (at 600 nm) of the chloroform phase containing ferrocene derivatives **1**−**5** (1 mM concentration) after equilibration with an aqueous solution containing β-SH-CD-capped gold nanoparticles (1 mg/mL) at 20 °C.

To obtain further evidence for the relevance of ferrocene-CD inclusion complexation at the nanoparticle−solution interface, we performed additional experiments adding a competing CD guest to the two-phase system. Specifically, we used adamantanol because this compound has reasonable solubility in the two phases used in this work. Our experimental results indicate that the presence of adamantanol in the system decreases the extent of nanoparticle phase transfer. In fact, the data in Figure 7A demonstrate that the concentration of transferred nanoparticles correlates inversely with the concentration of adamantanol added. These findings can be rationalized by a

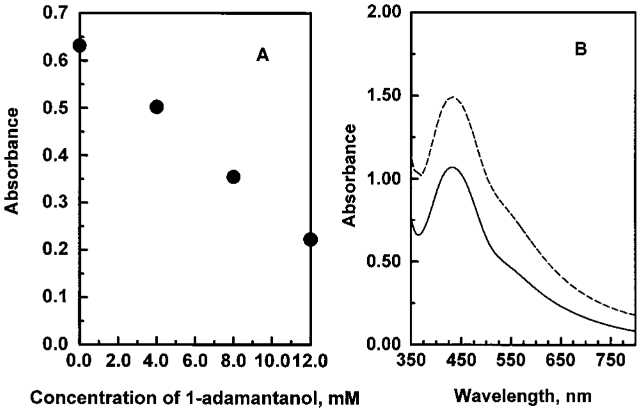


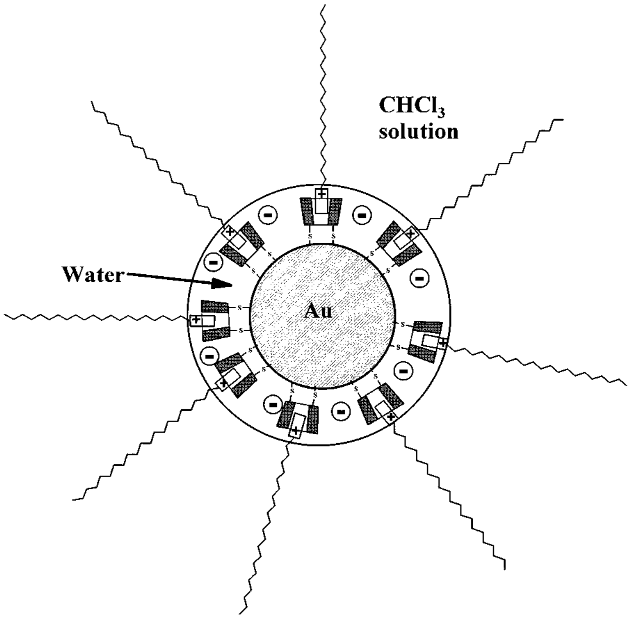
Figure 7. (A) Absorbance (at 600 nm) of the chloroform phase containing 4 mM **3** and variable concentrations of 1-adamantanol after equilibration with an aqueous solution of β-SH-CD-capped gold nanoparticles (0.4 mg/mL). (B) Visible spectrum of the chloroform phase containing 5 mM **3** after equilibration with aqueous solutions containing of β-SH-CD- (discontinuous line) and α-SH-CD-capped (continuous line) gold nanoparticles. The initial concentration of the gold nanoparticles in the water phase was 0.4 mg/mL in both cases.

simple model that takes into account the competitive binding of the ferrocene and adamantane derivatives in the CD cavities available on the nanoparticles. Of course, adamantanol binding is not productive in terms of phase transfer, as it does not afford the necessary hydrophobic character to the surface of the nanoparticles. Similar results were found when ferrocenemethanol was used as the competing guest, but the quantitative effects were smaller due to the lower binding constants with β-CD of ferrocene-containing guests compared to those of adamantane derivatives.[16]

Finally, we also compared the extent of phase transfer of β-SH-CD-capped nanoparticles with that of α-SH-CD-capped nanoparticles of similar size. Figure 7B shows the spectra of the organic phases resulting from these experiments. Clearly, the former type of nanoparticles is more effectively solubilized in the organic phase than the α-SH-CD-capped gold nanoparticles, under identical experimental conditions. This finding is in excellent agreement with the well-established selectivity of ferrocene derivatives[8f] for β-CD hosts compared to α-CD (or γ-CD) and provides additional support to the proposed involvement of nanoparticle/CD-ferrocene complexation in the phase transfer mechanism.

PCS measurements were also performed to investigate the possibility of interparticle aggregation in our experiments. Our PCS instrument can only detect light scattered by particles larger than 3 nm. Therefore, the CD-capped gold nanoparticles used in this work are undetectable, but their aggregation would be clearly observed in these experiments. First, CD-capped gold nanoparticles in aqueous media remain undetected by PCS for months, revealing their long-term stability and lack of aggregation. After equilibration with a chloroform solution of compounds **3**−**5**, no particles were detected by PCS in the chloroform solution. This result is not surprising if one considers that the organic layer created around the metal core of the particles offers little "contrast" with the chloroform phase, i.e., their refractive indexes are similar. Therefore, our PCS data provide support for the individual character of the nanoparticles in the chloroform phase and reject the notion that the particles may aggregate upon solubilization in the organic medium.

Scheme 2. Proposed Structure for the Assemblies Formed upon Transfer of the β-SH-CD-Capped Gold Nanoparticles into Chloroform Solution



It is well-known that CDs are very poor hosts for hydrophobic guests in nonaqueous media, especially in solvents of low polarity, such as chloroform. Therefore, we must ask: What holds our ferrocene derivatives "glued" to the CD cavities after transfer to $CHCl_3$? The only rational explanation is that, as the formation of inclusion complexes takes place in aqueous solution, water molecules are also transferred along with the nanoparticles into the chloroform solution. The presence of the positively charged nitrogen atoms in the vicinity of the ferrocene subunits probably assists in transferring water molecules and counterions to the organic phase. To obtain further evidence for the importance of water in the assemblies formed after phase transfer to $CHCl_3$, we performed the following experiment. A solution of nanoparticles in $CHCl_3$ was prepared with compound **5** as the phase transfer reagent. The chloroform solvent was allowed to evaporate and the solid residue was dried overnight at 60 °C under vacuum. After drying, the residue (CD-capped gold nanoparticles + compound **5**) was found to be insoluble in dry $CHCl_3$ but the solubility was restored when the chloroform was equilibrated with water. This finding clearly demonstrates that some water is necessary for the efficient phase transfer of the nanoparticles into $CHCl_3$. Thus, the proposed idealized structure of the nanoparticles after their transfer to the chloroform phase (Scheme 2) has some similarities with the structure of reverse micelles. We conclude that these nanoparticle-centered assemblies are conceptually similar to *gold-filled reverse micelles*.

Conclusions

This work has shown that CD-capped gold nanoparticles with average core diameters of ca. 3 nm act as effective hosts for cationic ferrocene derivatives, as evidenced by electrochemical and ^{1}H NMR spectroscopic data. Ferrocene derivatives **3**, **4**, and **5** act as phase transfer agents and efficiently solubilize the nanoparticles in chloroform solution. By contrast, ferrocene derivatives **1** and **2**, both having a very limited amphiphilic character, are ineffective as phase transfer agents. Our data suggest that the CD-capped nanoparticles template the formation of unusual assemblies in the chloroform solution, as each particle

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[16] Godínez, L. A.; Schwartz, L.; Criss, C. M.; Kaifer, A. E. *J. Phys. Chem. B* **1997**, *101*, 3376.

is surrounded by ferrocene amphiphiles, anchored to the nanoparticle by their CD-bound ferrocene residues, as well as water molecules and counterions.

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Supporting Information Available: Description of electrochemical results that support binding of **1** to CD-capped gold nanoparticles and additional UV−vis spectral data for the nanoparticles (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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