

Cyclodextrin-Modified Gold Nanospheres. Host–Guest Interactions at Work to Control Colloidal Properties

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Received February 3, 1999

Renewed interest in metal clusters and colloidal particles has given rise to an expanding area of interdisciplinary research.^{1–6} Most types of metal nanoparticles can be stabilized by a variety of organic materials. Mirkin and co-workers have shown that gold colloidal particles modified with oligonucleotides form large solution assemblies in which the colloidal particles are linked by binding forces between complementary oligonucleotide strands.¹ A range of molecular recognition interactions (some of them based on synthetic or nonbiological host/guest species) can be exploited to endow the metal nanoparticles with tailor-made properties. In this communication, we demonstrate that gold colloidal particles can be modified with molecular receptors (cyclodextrins⁷) that can be used to control particle aggregation via simple host–guest interactions.

Addition of *per*-6-thio- β -cyclodextrin (**1**) to a colloidal dispersion of gold nanoparticles⁸ (diameter: 12.5 ± 2.4 nm as determined by photon correlation spectroscopy (PCS) or 11.8 nm by SEM) results in the attachment of thiolated cyclodextrins to the gold particles. This was verified by several lines of evidence. First, the average size of the **1**-modified gold nanospheres increases slightly to 14.0 ± 2.5 nm, as measured by PCS (a technique sensitive to the diffusion coefficient of the particles), while it remains essentially unchanged (11.9 nm) by SEM (a

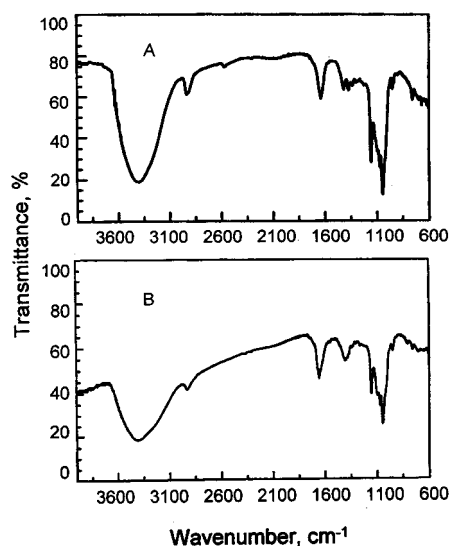
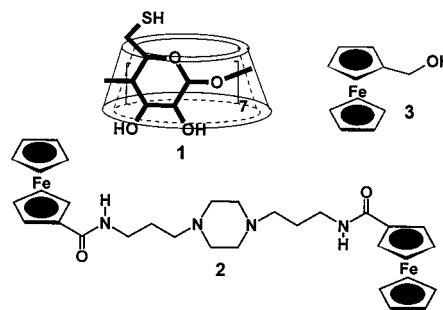


Figure 1. FT-IR spectra of (A) **1** in a KBr pellet and (B) **1**-modified gold colloidal particles in a KBr pellet. The modified colloidal particles were precipitated as described in ref 8, washed with 1 M NaCl to remove residual citrate, dried under vacuum, and mixed with KBr for pellet preparation.

technique that images the metallic core of the particles). Second, the visible spectrum of the gold colloidal particles exhibits a maximum for the surface plasmon resonance absorption at 520 nm. This maximum shifts to 526 nm (see Supporting Information) after surface modification with **1**.⁹ Third, the FT-IR spectrum of the **1**-modified gold nanoparticles strongly resembles that of free **1** (Figure 1). To the best of our knowledge, these experiments demonstrate for the first time the modification of gold colloidal particles with a synthetic molecular host.



After verifying the attachment of **1** to the gold nanospheres, we set out to investigate the effects that the particle-immobilized cyclodextrin receptors exert on the properties of the gold colloid. Specifically, we decided to exploit the well-known host–guest molecular interactions between β -CD hosts and ferrocene derivatives.¹⁰ We reasoned that the ferrocene dimer **2** should act as a

(8) The gold colloid was prepared following Natan's method (ref 5f). The gold colloidal particles were derivatized by adding **1** (14.4 mg) to 100 mL of the previously prepared gold colloid (~ 1 mM Au) and stirring in the dark for 2 days. To this dispersion, DMSO (50 mL) was added and stirred for 2 more days. The water was removed under vacuum at room temperature and acetonitrile (50 mL) added to precipitate a red solid that was collected by centrifugation and washed with DMSO–CH₃CN (1: 1). At this stage, complete removal of free **1** was verified by TLC. The precipitate was then redissolved in 100 mL of pure water and filtered through a 0.8- μ m Gelman membrane filter.

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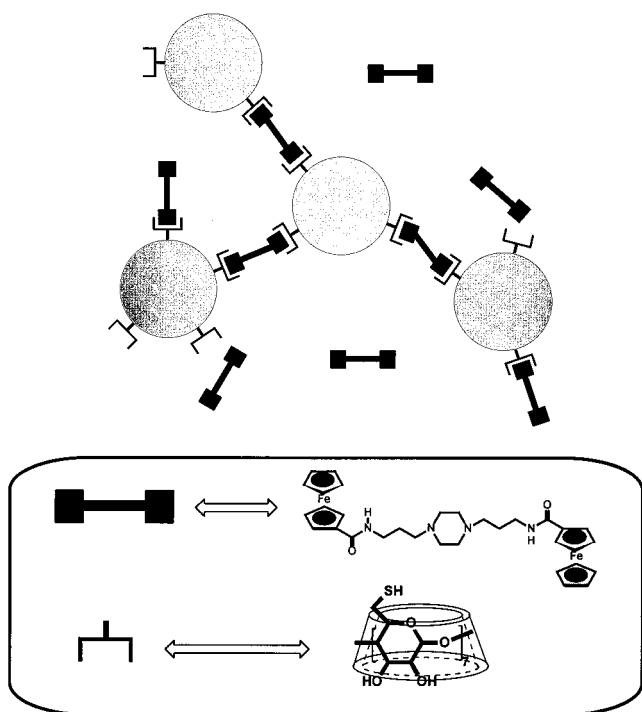
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Scheme 1



linker between different gold particles, leading to their aggregation (see Scheme 1). Indeed, addition of **2** (0.1 mM) to an aqueous colloidal dispersion of **1**-modified gold nanospheres¹¹ initially causes a red shift on the surface plasmon resonance absorption of the colloidal particles. Almost immediately, slow precipitation of a red solid takes place accompanied by the attenuation of the surface plasmon absorption (Figure 2). The red precipitate was isolated and analyzed by Energy Dispersive Spectroscopy (EDS). The major elemental component was found to be Au, as expected, but a small amount of Fe (from the ferrocene residues) was also detected. Treatment of the precipitate with CDCl_3 led to the unequivocal identification by ^1H NMR spectroscopy of dimer **2** as the only organic component of this material that can be easily extracted in this solvent (see Supporting Information).

In contrast to the results obtained with **2**, addition of ferrocene-methanol (compound **3**, 1.0 mM) to the aqueous dispersion of **1**-modified gold nanoparticles did not cause any precipitation or flocculation. Similarly, addition of 1,4-bis(3-aminopropyl)piperazine (0.5 mM), the tether between the two ferrocene subunits in **2**, had absolutely no effect on the stability of the modified colloidal particles. In a different type of control experiment, 0.1 mM **2** and 6 mM free β -CD were added to the dispersion of **1**-modified gold colloidal particles. Again, no precipitation or flocculation was observed (see Figure 2, inset) as the free CD hosts compete with the surface attached CD hosts for the available

(11) Under these conditions, the solution contains approximately 5×10^{15} Au particles and 6×10^{19} dimer molecules per liter. The rigid structure of the bridge between the two ferrocene residues in dimer **2** disfavors binding of the two ends to the same particle.

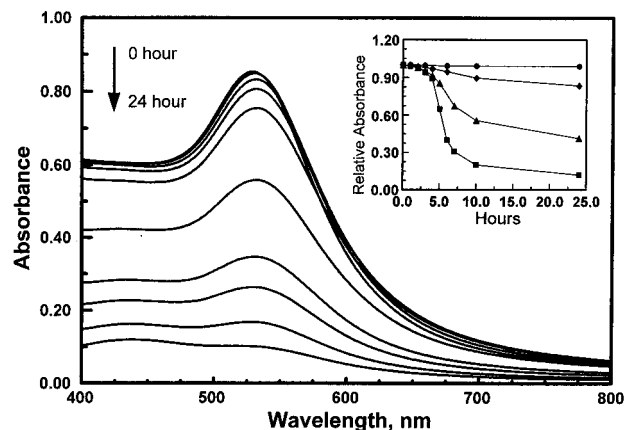


Figure 2. Time dependence of the visible spectrum of a **1**-modified colloidal dispersion after addition of 0.1 mM dimer **2**. Inset: Time dependence of the relative absorbance (at 526 nm) recorded after addition of (■) 0.1 mM **2**, (▲) 0.1 mM **2** + 0.1 mM β -CD, (◆) 0.1 mM **2** + 1 mM β -CD, and (●) 0.1 mM **2** + 6 mM β -CD.

ferrocene groups. This prevents flocculation since the dimers cannot form a significant number of linkages between nanoparticles. It is indeed possible to control the rate of flocculation by adjusting the concentration of free β -CD in the medium (Figure 2, inset). Alternatively, addition of 0.1 mM **2** and 1 mM **3** does not lead to any precipitation or flocculation, as **3** also interferes with the formation of interparticle linkages by dimer **2**.

The reversible character of the ferrocene- β -CD binding makes it possible to reverse the flocculation process. For instance, addition of 1 mM **3** to the solution in contact with **2**-induced, gold colloid flocculate leads to its partial redissolution.¹² We have also investigated the effect that the concentration of **2** has on the flocculation of **1**-modified gold nanoparticles. As expected, the kinetics of flocculation slows down as the dimer concentration decreases. Temperature also plays an important role. Increasing the temperature diminishes the extent of flocculation, probably due to the anticipated decrease of the binding constant between the ferrocene residues and the β -CD hosts. These effects will be described in more detail in a future publication. In summary, our experiments have clearly shown that gold colloidal particles can be readily modified with simple synthetic receptors, such as the thiolated cyclodextrin **1**. The receptor's binding properties can then be exploited to control in a predictable fashion the properties of the colloidal particles.

Acknowledgment. The authors are grateful to the National Science Foundation for the generous support of this work (to A.E.K., CHE-9633434). E.R. acknowledges a Maytag graduate fellowship from the University of Miami.

Supporting Information Available: Synthetic procedure for the preparation of **2**, visible spectra of unmodified and **1**-modified gold colloids, and ^1H NMR spectrum of the organic extract from the colloidal flocculate (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(12) We thank one of the reviewers for suggesting this experiment.