2007

Air and Water Free Solid-Phase Synthesis of Thiol Stabilized Au Nanoparticles with Anchored, Recyclable Dendrimer Templates

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Solid-phase synthetic templates for Au nanoparticles were developed using Merrifield resins and polyamidoamine (PAMAM) dendrimers. This synthetic scheme affords the opportunity to prepare metal nanoparticles in the absence of air and water, and it does not necessitate phase transfer agents that can be difficult to remove in subsequent steps. Amine-terminated generation 5 PAMAM (G5NH₂) dendrimers were grafted to anhydride functionalized polystyrene resin beads and alkylated with 1,2-epoxydodecane to produce G5C₁₂ anch. The anchored dendrimers bound both Co(II) and Au(III) salts from toluene solutions at ratios comparable to those of solution phase alkyl-terminated PAMAM dendrimers. The encapsulated Au(III) salts could be reduced with NaBH₄ to produce anchored dendrimer encapsulated nanoparticles (DENs). Treatment of the anchored DENs with decanethiol in toluene extracted the Au nanoparticles from the dendrimers as monolayer protected clusters (MPCs). After a brief NaCN etch, the anchored dendrimers were readily recycled and a subsequent synthesis of decanethiol Au MPCs was performed with comparable MPC yield and particle size distribution.

Introduction

Metal nanoparticles (NPs) are utilized in a wide variety of disciplines and can be employed as homogeneous or heterogeneous catalysts¹ as well as biological and molecular sensors.² A variety of NP synthetic strategies can be employed, but the most widely used methods utilize a simple metal salt, a reducing agent, and a colloid stabilizer. For example, the Schiffrin and Brust³ method involves a biphasic water-organic solvent system where the reduction of a metal salt (e.g., HAuCl₄ or Na₂PdCl₄) is performed in the presence of a colloid stabilizer (typically an alkyl thiol or (4-dimethylamino)pyridine) and a phase transfer reagent such as [N(C₆H₄Me)₂]Br. When NaBH₄ is added this suspension, the alkyl thiol serves to arrest nanoparticle growth and carry the reduced metal particle into the organic solvent. Careful control over reagent concentrations allows for substantial control over particle sizes and dispersity.

Polymers such as polyvinylpyrrolidone (PVP) and poly(ethylene glycol) can be employed as colloid stabilizers in similar preparative schemes.² Starburst polyamidoamine (PAMAM) dendrimers are a specific class of nearly monodisperse, hyperbranched polymers that have been used to template nearly monodisperse nanoparticles. PAMAM dendrimers, which have open interiors and porous peripheries, serve as both particle templates and stabilizers and can be used in preparing a wide variety of mono- and bimetallic metal NPs.⁴,⁵ In this synthetic scheme, metal precursors are first bound to the interior amine groups of the PAMAM dendrimer; addition of a reducing agent prepares particles that are essentially trapped within the dendrimer interior. The dendrimer mediated synthesis allows for greatly increased control over particle size and composition relative to traditional colloid preparation methods. For bimetallic particles, well-mixed and core-shell particles on the order of 2 nm in diameter can be selectively prepared.

Because PAMAM dendrimers can terminate in a wide variety of end groups (—OH, —NH₂, and alkyl chains), they can be soluble in either polar or nonpolar solvents, making air and water free⁶—⁸ syntheses tractable. This is especially important for metals that are readily oxidized.¹⁰ Additionally, Au, Pd, and Ag nanoparticles can be extracted from the dendrimer interior using an appropriate thiol or carboxylate to prepare monolayer protected clusters (MPCs) that are similar to nanoparticles prepared by the Schiffrin and Brust method. Thus, nanoparticles can be prepared in aqueous solution and extracted into organic solvents and vice versa⁹,¹¹ (see Scheme 1). This two-phase synthesis provides for substantial flexibility in the synthetic methodologies, a rapid means of eliminating byproducts from the metal reduction step, and allows for recycling of the expensive dendrimer template.

The requirement of aqueous solvents either during metal complexation and reduction or during extraction is a substantial drawback to the Brust-type and dendrimer mediated synthetic schemes. In addition, phase transfer agents can be difficult to isolate from reaction products and are therefore problematic contaminants in Brust-type syntheses.¹² Aqueous solvents are particularly problematic for oxidizable metals, where water or air can cause substantial changes in nanoparticle structure or

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and various resins\textsuperscript{29,30} for the purpose of immobilizing catalysts onto solid supports.\textsuperscript{31–33} One particular study investigated Pd NP catalysts templated on hyperbranched polymers constructed on mesoporous silica.\textsuperscript{34} From the perspective of nanoparticle synthesis, these approaches have substantial drawbacks. The support superstructure often limits the size of dendrimer available (generation 4 or higher dendrimers are preferable for nanoparticle synthesis). Additionally, the materials are extremely time-consuming to prepare, and it is difficult to ensure that the dendritic materials prepared on the supports are comparable to those in solution.

We reasoned that if it were possible to attach (instead of synthesizing) the NP template/stabilizer (dendrimer) to a solid support (resin bead), then it would be possible to carry out the synthesis and extraction of NPs entirely in nonaqueous solvents with relative ease. Our long-term goals are to develop dendrimer mediated synthetic routes to bimetallic Au based nanoparticles and catalysts, particularly for oxidizable first row transition metals. Since there are no appropriate air and water free synthetic routes to Au MPCs, we initially embarked on a proof of concept study to show that the synthesis of monometallic Au MPCs is possible using anchored dendrimers. The details of that study are reported here.

**Experimental Section**

**Materials and Reagents.** MP-anhydride resin (7.4 mmol anhydride/g resin) was purchased from EMD Biosciences and used as received. Amine terminated generation 5 polyamidoamine (PAMAM) and dodecanol terminated (50%) generation 5 PAMAM dendrimers were purchased from Dendritech. H\textsubscript{2}AuCl\textsubscript{4} (Alfa), CoCl\textsubscript{2}-6H\textsubscript{2}O (Aldrich), and decanethiol (Aldrich) were used as received. Reagent grade toluene, methanol, and dimethylformamide (DMF, Fischer) were dried under molecular sieves (Davison, Grade 564, 3 Å) and otherwise used as received. DMF-d\textsubscript{6} and CD\textsubscript{3}OD (CIL) were used as received. Water was purified to a resistivity of 17–18 MΩ cm with a Barnstead Nanopure system.

**Characterization.** Solution UV–visible absorbance spectra were collected on a Jacso–V–530 spectrometer using quartz cells. Reflectance UV–visible spectra were collected on an Ocean Optics UV–visible-NIR spectrometer equipped with a reflectance probe using the appropriate solid support as the reference. \textsuperscript{1}H NMR spectra were recorded on a Varian Unity/Inova 400 spectrometer at an operating frequency of 399.96 MHz. The \textsuperscript{1}H chemical shifts were referenced to internal solvent peaks. Transmission electron microscope (TEM) analysis of the nanoparticles was performed with a JEOL 2010F instrument operating at 200 kV. Nanoparticles suspended in hexane were drop cast onto a 150 mesh Cu TEM grid covered with a thin amorphous carbon film. Image analysis was performed with DigitalMicrograph 3.6.1 (Gatan) software. Elemental analyses were performed by Desert Analytics (Tucson, AZ). Attenuated total reflection Fourier transform infrared (ATR-FTIR) spectra were collected on a Thermo-Nicolet Nexus 470 FT-IR instrument using a Smart Golden Gate ATR accessory. Atomic absorption spectroscopy was performed on a Varian Spectra AA

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\textsuperscript{17} Jana, N. R.; Peng, X. J. Am. Chem. Soc. 2003, 125, 14280–14281.


\textsuperscript{26} Dahan, A.; Portnoy, M. Org. Lett. 2003, 5, 1197–1200.


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Briefly, the samples were digested in fresh aqua regia at 60 °C for 3 h. The solution pH was adjusted to 4–6 before the samples were analyzed. MPC samples were purified three times (see the Experimental Section) and subsequently treated in a vacuum oven at 80 °C overnight (to remove most of the thiol) before being dissolved in aqua regia.

**Dendrimer Anchoring and Alkylation.** MP-anhydride dendrimer (600 mg; 4.44 mmol anhydride) was swelled in 5 mL of DMF-d₆ for 1 h, producing a 4.5 μM slurry of G5C₁₂₃₄₅. To that mixture, either 1051 or 2813 μL of 4.7 mM HAuCl₄ in ethanol was added to give a 55:1 or 147:1 Au/dendrimer molar ratio, respectively. The beads and HAuCl₄ were allowed to stir for 1 h and then were filtered, rinsed with 10 mL of toluene (3 ×), and redispersed in 20 mL of fresh toluene. Freshly prepared 50 mM NaBH₄ in methanol (2000 μL) was then added to the stirring beads, instantly changing their color from yellow to brown.

**Preparation of Au Dendrimer Encapsulated Nanoparticles (DENs).** G5C₁₂₃₄₅ (0.09 μmol; 200 μL of 0.45 nmol G5C₁₂₃₄₅/mg bead) was stirred in 20 mL of toluene for 1 h, producing a 4.5 μM slurry of G5C₁₂₃₄₅. To that mixture, either 1051 or 2813 μL of 4.7 mM HAuCl₄ in ethanol was added to give a 55:1 or 147:1 Au/dendrimer molar ratio, respectively. The beads and HAuCl₄ were allowed to stir for 1 h and then were filtered, rinsed with 10 mL of toluene (3 ×), and redispersed in 20 mL of fresh toluene. Freshly prepared 50 mM NaBH₄ in methanol (2000 μL) was then added to the stirring beads, instantly changing their color from yellow to brown.

**Extraction and Purification of Au Nanoparticles from the G5C₁₂₃₄₅.** The above mixture containing the anchored DENs was decanted, and 10 mL of toluene was added to the beads with vigorous stirring (magnetic stir bar with stirrer set on high). Freshly prepared 50 mM NaBH₄ in methanol (1000 μL) was added, followed instantly by 3000 μL of decanethiol in 5 mL of toluene. The solution turned colorless to brown after 5 min, but it was allowed to stir for at least 2 h, yielding a brown solution of extracted Au MPCs. The toluene solution containing the MPC product was purified by first concentrating the solution to 1 mL on a rotary evaporator and then adding 15 mL of ethanol to precipitate the MPCs. Centrifugation resulted in the separation of the MPCs from excess free -alkanethiol and other impurities. The MPCs were washed and centrifuged twice and other impurities. The MPCs were washed and centrifuged twice.

**Results and Discussion**

**Anchoring of the G5NH₂/PAMAM Dendrimer to Polystyrene Resin Bead(s).** To develop a synthetic methodology appropriate for the air and water free synthesis of metal thiol stabilized metal nanoparticles, we explored the strategy shown in Scheme 2. Essentially, we drew from existing dendrimer immobilization techniques by reacting fifth generation amine terminated PAMAM dendrimers (G5NH₂) with anhydride functionalized polystyrene Merrifield resin beads. The reaction proceeds quickly and cleanly when 100-fold excess of anhydride to terminal amine groups is used, and the beads are readily filtered after reaction for 12 h. Figure 1 shows the ¹H NMR spectrum of the reaction solution (DMF-d₆/CD₂OD) before and after the reaction. The diagnostic resonances attributed to the methylene protons of G5NH₂ from 2.2 to 3.4 ppm are present in the spectrum of the starting material. After the reaction, these resonances have disappeared, indicating that G5NH₂ has been removed from solution.

Figure 2 presents infrared spectra of the amide and carbonyl region of the beads before and after reaction. The peaks at 1822 and 1746 cm⁻¹ in Figure 2a correspond to the amide carbonyl bands of the resin beads. The intense carbonyl band at 1746 cm⁻¹ in Figure 2a corresponds to the amide carbonyl bands of the resin beads. The sharp resonance at 1746 cm⁻¹ in Figure 2a corresponds to the amide carbonyl bands of the resin beads. The intense carbonyl band at 1746 cm⁻¹ in Figure 2a corresponds to the amide carbonyl bands of the resin beads.

**Figure 1.** ¹H NMR spectra of the reaction mixture (DMF-d₆/CD₂OD) of MP-anhydride resin and G5NH₂ (a) before and (b) after reaction. The sharp resonance at 3.16 ppm arises from an impurity in the resin beads.

**Figure 2.** ATR-FTIR spectra of MP-anhydride resin (a) before reaction, (b) after reaction with G5NH₂, and (c) after alkylation with 1,2-epoxydodecane.
those bands decreases after the reaction with G5NH₂, while new peaks at 1723, 1661, and 1560 cm⁻¹ appear. The peak at 1723 cm⁻¹ is assigned to the carbonyl band of the carboxylic acid produced from reaction with the dendrimer and from methanolysis. The appearance of the amide I and II peaks at 1661 and 1560 cm⁻¹, respectively, arises from both the internal amides of G5NH₂ as well as the amide bonds formed by reaction with the anhydride bead(s). Thus, the IR data confirm covalent attachment of the dendrimer via amide bond formation and not simple adsorption.³⁸,⁴¹

The primary goal of developing air and water free synthetic routes to metal nanoparticles necessitated modification of the anchored dendrimers so that they are more compatible with organic solvents. Consequently, the surfaces of the anchored dendrimers were rendered hydrophobic by reacting the remaining (unreacted) primary amines with 1,2-epoxydocadecane (eq 1), producing G5C12anch.

This alkylation was performed to provide additional steric bulk to the dendrimers and ensure that the more polar PAMAM dendrimer superstructure would not collapse upon itself in nonpolar solvents.⁴³ This also allowed us to mimic the solution chemistry of G5C12 and prevent linking of the dendrimers through the addition of metal ions.⁴⁺⁴⁴

¹H NMR of the epoxide solution (see the Supporting Information) indicates that this reaction proceeds to ~50% completion based on the ratio between added epoxide and primary amine groups. This value is consistent with those of commercially available G5⁺ PAMAM dendrimers; as the generation increases, it becomes more difficult to completely react the end groups. Additionally, some of the surface amines associated with and near the points of attachment between the dendrimer and the resin bead are expected to be inaccessible to the alkylating agent (either due to steric hindrance or to potential protonation during the anchoring reaction). Figure 2c also shows that the few remaining bead anhydride groups on the beads are passivated through these treatments. The bands at 1822 and 1746 cm⁻¹ in the carbonyl region are completely replaced with a band at 1723 cm⁻¹, which is assigned to carboxylates formed through methanolysis.

**Metal Uptake by the Anchored Dendrimers.** In evaluating the anchored hydrophobic dendrimers as nanoparticle templates in organic solvents, it was first necessary to confirm that their capacity for binding metal complexes is not destroyed by the anchoring process. Due to its relatively high extinction coefficient in organic solvents (~10³ M⁻¹ cm⁻¹), CoCl₂ was chosen to probe metal complexation by G5C12anch.⁴⁵ Figure 3 shows solution UV-visible spectra of Co⁺ and Co⁷⁺ + G5C12 and a reflectance spectrum of Co⁺ + G5C12anch. The 500⁻⁷00 nm region in the electronic spectrum exhibits the characteristic multicomponent band associated with the 4A₂ → 4T₁ transition in tetrahedral or pseudotetrahedral Co⁰ complexes.⁴⁶ The λmax for this band undergoes a significant red shift (~50 nm) when Co⁰ is added to a toluene solution of G5C12. This is presumably due to the encapsulation of Co⁷⁺ into the dendrimer interior. When a solution of 550 μmol CoCl₂ is stirred with 10 μmol G5C12anch in toluene, the solution turns colorless, while the beads change from off-white to blue-green. Control experiments using CoCl₂ and unmodified resin beads resulted in no coloration of the beads. The reflectance UV-visible spectrum in Figure 3 shows that the peak corresponding to encapsulated Co⁰ is present in the filtered and dried G5C12anch, indicating that the Co⁷⁺ ions are indeed encapsulated in the G5C12anch in a similar fashion as in a toluene solution of G5C12.

Figure 4 shows a spectrophotometric titration of G5C12anch with Co⁰. This experiment is facilitated by the anchoring because the solution stays colorless as the Co⁰ is encapsulated into the G5C12anch. When more than 150 equiv of Co⁰ is added, the solution turns blue and gives a UV-visible spectrum identical to that of Co⁰ in solution. This value is slightly greater than the number of tertiary amines present in the dendrimer (126); there

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(41) Determination of the dendrimer loading by elemental analysis of the anchored dendrimer beads was undiagnostic due to the residual nitrogen content in the parent beads (0.74%). The theoretical %N of 4.5E⁻⁰⁴ mol/dendrimer loading was calculated to be 0.48%.


(45) Although Au⁰ has a high extinction coefficient in the UV, it is difficult to resolve this band due to the dendrimer. Additionally, Au⁰ begins to oxidize to Au¹⁻ and Au²⁺ terminated PAMAM dendrimers over the course of several minutes (see ref 44). The combination of these two factors makes it very difficult to accurately determine Au—dendrimer stoichiometries for the anchored dendrimers. The Co⁰ titration is used instead, as it is experimentally straightforward and allows us to directly compare metal uptake by anchored dendrimers to that by solution phase dendrimers.

are an additional 128 “surface” primary and secondary amines due to the alkylation step. This value is in good agreement with that of the CoIII encapsulation capacity of G5C12 in solution, which was determined to be 165 equiv (see the Supporting Information).

**Air and Water Free Preparation of Au DENs.** The essence of this study was to develop a synthetic procedure suitable for the air and water free preparation of metal nanoparticles. As such, we prepared Au MPCs as a critical proof of concept for the synthetic strategy. The Au DENs were prepared by adding HAuCl4 in ethanol to a toluene slurry of G5C12 anch using either a 55:1 or 147:1 Au/dendrimer ratio. The solution turned colorless, and the beads turned pale yellow over a period of 1 h. The reflectance UV–visible spectrum of the filtered and dried Au55:1 or 147:1 DENs is similar to the solution UV–visible spectrum of G5C12(Au55)0.5, indicating that the Au is encapsulated within the dendrimer (see the Supporting Information). The nomenclature used is consistent with that utilized for Au DENs and MPCs and indicates the metal/dendrimer ratio used in the synthesis rather than the ultimate cluster size.

Addition of NaBH4 to the slurry caused the beads to turn from pale yellow to brown, which is characteristic of Au DENs.4 As Figure 5 shows, the reflectance UV–visible spectrum of the filtered and dried G5C12anch(Au147) shows the monotonic increase in absorbance with decreasing wavelength that is characteristic of Rayleigh scattering by nanoparticles.47 An additional small absorption band appears as a shoulder, which is attributable to the surface plasmon band. The reflectance UV–visible spectrum of the filtered and dried G5C12anch(Au147)55 is very similar (see the Supporting Information) and will be discussed below.

To confirm that the anchored dendrimers template nanoparticles as they do in solution,4,5,11 two sets of control experiments were performed. First, when stirred with HAuCl4, unmodified resin beads showed no metal uptake over the course of 6 h. In a second comparable control experiment, G0NH2 was anchored to the MP-anhydride resin and alkylated with 1,2 epoxydodecane (see the Supporting Information). When stirred with AuIII in a comparable stoichiometry to that of G5C12anch G0C12anch bound only a small fraction of the metal. After reduction, the UV–visible reflectance spectrum of the filtered beads contained a very large plasmon band, indicating the presence of large Au particles (ida infra). No Au MPCs were produced or extracted upon vigorous stirring with decanethiol, which is similarly indicative of the presence of large nanoparticles trapped in the polystyrene (vida infra). The combination of these control experiments demonstrates that the G5C12 anch is indeed responsible for the NP templating. TEM images of the anchored DENs prior to extraction were collected, and they are available in the Supporting Information. Unfortunately, the size/thickness of the resin bead support prevents the observation of conclusive TEM evidence for the size of the NPs in the G5C12anch(Au55) samples prior to extraction. In a sense, the bead acts like an undried drop of the casting solvent, surrounding the particles with a variable layer of organic material that makes imaging small nanoparticles, which have relatively low electron densities, difficult. At the same time, large Au agglomerates, which would be far easier to image, were not observed, suggesting that the anchored DENs consist of small nanoparticles.

**Extraction of Au MPCs.** Beyond the utility of developing solid-phase synthetic procedures for nanoparticles, the conversion of Au DENs to Au MPCs affords the opportunity to prepare Au (and ultimately Au based bimetallic) nanoparticles in the absence of both water and air. The addition of 100-fold molar excess of decanethiol to toluene slurries of freshly reduced G5C12anch(Au55) (where n = 55 or 147) resulted in the solutions changing from colorless to brown.48 The solution UV–visible spectrum of the extracted Au147 MPC solution shown in Figure 5 is comparable to spectra reported by Crooks’ group.4,5,11 The plasmon band that was present in the reflectance spectrum for the G5C12anch(Au55) DENs is diminished significantly, indicating that the extracted Au NPs are smaller than 3 nm.49 The TEM micrographs and particle size distribution histograms in Figure 6 show an average diameter of 2.5 ± 0.5 nm, confirming this result. Results with Au55 MPCs are similar (2.0 ± 0.7 nm), and a TEM micrograph, particle size distribution histogram, and solution UV–visible spectrum of the Au55 MPCs can be found in the Supporting Information. AA spectroscopy of the MPC solutions indicates that the overall yield for the synthesis is 55% (based on the initial amount of HAuCl4 used).

In both cases (Au55 and Au147), the extracted particles are slightly larger than those reported by Crooks’ group.4,5,11 The resin bead prevents conclusive TEM evidence for the size of the NPs in the G5C12anch(Au55) samples (ida supra); however, the UV–visible spectra of G5C12anch(Au55) and G5C12anch(Au147) are similar, which suggests comparable particle sizes prior to extraction. Further evidence for particle growth during the extraction can be found in the beads themselves, which develop a purple tint during extraction. This suggests that some Au remains on the beads as larger particles; atomic absorption spectroscopy confirmed this conjecture, showing that approximately 18% of the Au used in the synthesis remained on the bead. Figure 7 shows the reflectance UV–visible spectrum of the beads before and after extraction. The anchored DENs have only a very weak plasmon band; however, the extracted beads show a larger plasmon band than that present in the anchored DENs. Miyake’s group has previously shown that the plasmon band intensity increases with particle size,50 supporting the conclusion that the larger Au particles are formed and subsequently trapped inside the beads during extraction.

Crooks’ group has previously established that thiol extraction (aqueous vs. organic phase) can have a dramatic effect on the particle size if insufficient thiol is used.11 Specifically, during extraction, the nascent MPCs are susceptible to aggregation if

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the particles are not fully passivated. It is therefore important to use a thiol/Au mole ratio of at least 100 to drive the Au-thiol binding kinetics and facilitate extraction without agglomeration. In aqueous-organic extractions, the NPs are completely extracted from the dendrimer in approximately 1 min, while NP extraction from G5C12anch takes 5–120 min.

Crooks’ group reported that two-phase aqueous-organic extractions are performed by shaking in a separatory funnel by hand, while the single-phase extractions for G5C12anch reported here are performed by adding the thiol directly to the toluene phase under vigorous stirring with a magnetic stir bar. This gives the aqueous-organic extractions much larger surface contact between the DENs and thiol layers than is possible with the beads, and it may account for the differences in extraction times and particle size distributions. Additionally, extraction in the two-phase method is facilitated by the addition of excess NaBH4 to the aqueous solution immediately before extraction. This ensures that the Au nanoparticle surface is freshly reduced and increases the ionic strength of the aqueous solution, thus “opening up” the dendrimer. In the case of the solid-phase extraction, an excess of NaBH4 in methanol is used as a substitute since solid NaBH4 is not soluble in toluene. This may also account for some particle agglomeration; however, it should be noted that in organic to aqueous extractions9 no extra NaBH4 is required. Finally, it also cannot be ruled out that the broader particle size distributions observed for the solid-phase synthesis are a consequence of the nascent MPCs having a difficult time escaping from the dendrimer interior, causing a degree of agglomeration or aggregation within the pores of the beads.

Since these larger particles are formed during extraction, further refinements to this synthetic step may improve the overall dispersity of the MPCs. Although refining the extraction procedure may lead to slightly smaller particle sizes and more narrow distributions, the anchored dendrimers clearly accomplish the goal of this work: they are viable templates for the preparation of...
of relatively small nanoparticles in the absence of both water and air. Additionally, this new synthetic scheme requires much weaker reducing agents than those of other single-phase nanoparticle preparation methods.\textsuperscript{10-13} Evaluating potential improvements to the scheme is nonetheless useful in evaluating and ultimately refining the synthetic methodology. The bead pore structure appears to play a key role, so employing resins or supports with larger, well-defined, and more accessible pore structures should facilitate thiol access to the NPs and reduce the degree of agglomeration. It may also be possible to improve particle size distributions by using shorter chain alkyl thiols or by employing more vigorous mixing methods (e.g., vortexing). Current work in our lab is directed toward implementing these refinements and extending this templating scheme to additional metal systems.

**Recyclability of G5C12\textsubscript{anch}.** In addition to the exclusive utilization of nonaqueous solvents, another advantage of an anchored system is the possibility of rapidly and easily recycling the dendrimer. To recycle the anchored dendrimer, the unextracted Au was first etched using aqueous NaCN.\textsuperscript{51,52} Reflectance UV–visible spectra of G5C12\textsubscript{anch} before and after etching, shown in Figure 7, indicate that the G5C12\textsubscript{anch} is free of residual Au after the etch.

The G5C12\textsubscript{anch} was then used to synthesize a second batch of Au\textsubscript{147}. Figure 8 shows that the UV–visible spectra of the successive Au\textsubscript{147} MPC extractions are essentially identical. TEM micrographs and particle size distribution histograms of the two samples are shown in Figure 6. Both samples are nearly identical in both particle size and distribution (2.5 ± 0.5 and 2.5 ± 0.6 nm, respectively). The MPC yield from this second synthesis (46%) was comparable to the yield from the fresh sample, but it was slightly lower.

**Conclusions**

We have shown that it is possible to utilize solid-phase synthesis techniques to prepare small (<3 nm), fairly monodisperse Au NPs exclusively using organic solvents. The development of this preparative scheme is important because it affords opportunities to develop new synthetic routes to metal nanoparticles in the absence of air, water, and difficult to remove phase transfer agents. As a proof of principle, we prepared Au MPCs, which also allowed us to compare this new synthetic scheme to existing methodologies. This was accomplished by first anchoring fifth generation PAMAM dendrimers to anhydride functionalized polystyrene resin beads. The dendrimers were then alkylated, and their propensity to encapsulate metal ions was demonstrated by Co\textsuperscript{II} titrations. Au DENs were then synthesized and extracted as MPCs in the same solvent from which they were prepared (toluene). The measured particle sizes were slightly larger than predicted for Au\textsubscript{147} and Au\textsubscript{55} NPs; however, the particle sizes and distributions compare favorably with those prepared by Brust–Schiffrin and related methodologies. The key advance here is that the anchored dendrimer method eliminates the need for a biphasic synthesis with water, eliminates the use of difficult to remove phase transfer agents, and requires weaker reducing agents than comparable single-phase nanoparticle syntheses. In addition, the anchored, alkylated dendrimers were also shown to be recyclable in the synthesis of Au NPs of nearly identical size and distribution as those of the first batch.

**Acknowledgment.** The authors gratefully acknowledge the Robert A. Welch Foundation (Grant Nos. W-1552 and F-1529) and the U.S. National Science Foundation (Grant No. CHE-0449549) for financial support of our work.

**Supporting Information Available:** Experimental details for the \textsuperscript{1}H NMR determination of the alkylation reaction of G5NH\textsubscript{2}, Co\textsuperscript{III} titration of G5C12 in toluene, G0NH\textsubscript{2}anch synthesis and reactions, as well as representative UV–visible spectra, TEM images, and particle size distribution for Au\textsubscript{55}. This material is available free of charge via the Internet at http://pubs.acs.org.

LA7013573

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Supporting Information

Solid Phase Synthesis of Soluble Nanoparticles with Anchored, 
Recyclable Dendrimer Templates

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**Determination of the reaction yield of 1,2-epoxydodecane with G5NH2anch.**

To a freshly prepared solution (5 mL DMF-$d_6$ + 3 mL CD$_3$OD) of 2.0 g (1.2 µmol) G5NH$_2$anch, 75 µmol toluene was also added as an internal standard and allowed to shake at 50 rpm in a sealed vessel at 45 °C for 2 hours (to account for any loss due to swelling of the beads). After two hours, 30.0 mg (163 µmol) 1,2-epoxydodecane was added and an aliquot was immediately analyzed by $^1$H NMR. The solution was then shaken at 50 rpm in a sealed vessel at 45 °C for 48 hours and analyzed by $^1$H NMR every 24 hours. The resonances at 2.6 ppm (1,2-epoxydodecane) and 7.2 ppm (toluene) were integrated and compared to determine ~ 50% coverage of G5NH$_2$anch by 1,2-epoxydodecane to produce G5C12$_{anch}$ after 48 hours.

**UV-Vis titration plot of Co$^{II}$ complexation by G5C12 in solution.** In a quartz UV-Vis cuvette, 5 mL of a 2.2 µM solution of G5C12 in toluene was stirred. To that solution, 17 µL of an 8.4 mM solution of CoCl$_2$·6H$_2$O in EtOH was added every 5 minutes with stirring. A UV-Vis spectrum of the solution was collected after each aliquot (up to 400 equivalents Co$^{II}$) was added.

**G0NH2 anchoring and alkylation.** 500 mg M$p$-anhydride resin (3.70 mmol anhydride) was swelled in 5 mL DMF for one hour, followed by addition of 6 mg G0NH$_2$ PAMAM dendrimer (0.122 µmol) dissolved in 3 mL CH$_3$OH. The vessel was sealed, placed in a shaker at 50 rpm, and heated at 45 °C for 12 hours. The anchored amine terminated dendrimer is denoted G0NH$_2$anch.

To the above solution 12.0 mg (65.1 µmol) 1,2-epoxydodecane was added. The solution was shaken at 50 rpm in a sealed vessel at 45 °C for 48 hours. After reaction, the
beads were filtered, rinsed with MeOH, and allowed to dry in a vacuum oven at 40 °C overnight. The alkylated G0NH2-anch is denoted G0C12-anch.

**Encapsulation and reduction of AuIII with G0C12-anch.** 200 mg of alkylated anchored dendrimer beads (G0C12-anch) containing an average dendrimer loading of 4.65 µmol were stirred in 20 mL toluene for one hour. To that mixture, 3 mg of HAuCl₄ in 1 mL of EtOH was added to the solution to simulate a 55:1 Au:dendrimer molar ratio, respectively. This simulated ratio is based on the # of primary amines present (which is the same as in the G5C12-anch) allowing comparison of the respective templating ability of the two different generation of dendrimers. The beads and HAuCl₄ were allowed to stir for one hour and then were filtered, rinsed with 10 mL (3x) toluene, and redispersed in 20 mL fresh toluene. 2000 µL of a freshly prepared 50 mM NaBH₄ in MeOH was then added to the stirring beads, instantly changing their color from yellow to purple.

**Extraction of Au nanoparticles from the G0C12-anch.** The above mixture was decanted and 10 mL of toluene containing 3000 µL decanethiol was added to the beads with vigorous stirring. The solution remained colorless, and the beads remained purple, after stirring for 24 hours. No extraction was observed.
Figure S1. $^1$H NMR spectrum of the reaction mixture between G5NH$_2$anch and 1,2-epoxydodecane after 48 hours. The resonance at 7.2 ppm corresponds to an internal standard of 75 µmol toluene. The resonance at 2.6 ppm is attributed to one proton on the unreacted 1,2-epoxydodecane.

Figure S2. Titration plot of Co$^{II}$ uptake by 2.2 µM G5C12 with in solution. The intersection point corresponds to ~165 equivalents of Co$^{II}$ per dendrimer.
Figure S3. UV-visible spectra of solutions of 200 µM H\text{AuCl}_4 (blue line) and G5C12\text{(Au}^{\text{III}}\text{)}_{147} (red line) in EtOH/toluene. The black line is a UV-visible reflectance spectrum of filtered and dried H\text{AuCl}_4 and G5C12\text{anch}.

Figure S4. UV-Vis reflectance spectra of G5C12\text{anch(Au}^{\text{III}}\text{)}_{55} (black) and G5C12\text{anch(Au}_{55}\text{)}\text{DENs} (blue), as well as a solution UV-Vis spectrum of (C}_{10}\text{SH})\text{Au}_{55} \text{MPCs (red). The black line with no absorbance is a UV-Vis reflectance spectrum of filtered and dried resin beads that were stirred with H\text{AuCl}_4 (no Au}^{\text{III}}\text{ uptake).}
Figure S5. TEM image of (C$_{10}$SH) Au$_{55}$ MPCs synthesized from G5C12$_{anch}$. The corresponding particle size distribution (100 particles) is also shown. Note: the larger and somewhat bimodal particle size distribution may indicate that the anchored dendrimers are less effective at templating smaller particles, or that the extraction is less effective for the smaller metal:dendrimer ratio.

Figure S6. TEM images of G5C12$_{anch}$(Au$_{147}$) pre extraction. Note the presence of dark spots approximately ~2-3 nm in size.