

Fabrication of Water-Soluble Gold Nanoparticle Aggregates

by

Samantha E. Bennett

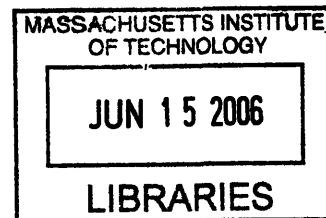
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ABSTRACT

Mixed monolayer protected gold nanoparticles were linked using octanedithiol to form aggregates containing hundreds of nanoparticles. These aggregates are an interesting material, posing potential applications in the fields of chemistry, biology and materials science. This study examined the dependence of aggregate size and morphology on temperature of formation, using AFM and TEM imaging. The aggregates formed at 70°C averaged 105nm in width, as compared to 70nm for the room temperature aggregates. The TEM images showed increased density for the 70°C aggregates. In a further study, the room temperature aggregates were functionalized through a place exchange reaction with 11-mercapto-undecane-1-sodiumsulfonate (MUS), a thiolated ligand with a polar head group. A two-phase test of the water-solubility indicated that the aggregates were fully soluble. TEM images showed a slight increase in size, though similar morphology to the insoluble aggregates. The ability to induce water solubility in the aggregates opens up many potential applications in the field of bionanomaterials.

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Chapter 1. Introductory Remarks

The study of metal-core nanoparticles has led to the discovery of their size-dependent electronic, magnetic and optical properties¹. Their use in catalytic and biomedical applications depends on our ability to stabilize and isolate the nanoparticles. Using phosphine-stabilization of Au₅₅ clusters, Schmid *et al* examined the properties of quantum-dot particles for the first time². Subsequent work established the Brust-Schiffrin model as the standard for stabilization of metal nanoparticles³. This technique provides a simple method using a self-assembled monolayer of thiolated ligands on the nanoparticle surface to prevent the particles from coalescing. These monolayer-protected metal nanoparticles (MPMNs) can be repeatedly isolated and redissolved in organic solvents without showing decomposition or irreversible aggregation⁴.

Self-assembled monolayers (SAMs) of thiolated ligands provide an easy and convenient method by which to control the interfacial properties of metal nanoparticles⁵. Recent work using a mixture of thiolated ligands has shown phase separation resulting in ordered domains. Using two types of thiols, “ripples” are observed that encircle the nanoparticle, with widths as small as 5 Å⁶ [Figure 1]. These and other novel MPMNs have potential applications as nanoscale electronic devices, multifunctional catalysts, and chemical sensors⁷. Further functionalization of the SAMs can be realized through place exchange reactions of the thiolated ligands⁸.

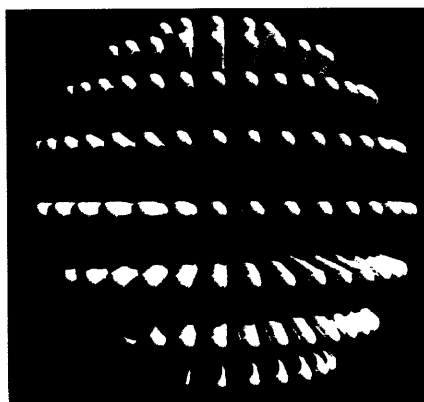


Figure 1. Schematic showing phase separated ligands on a rippled nanoparticle⁶.

The assembly of nanoparticles into controlled sizes and shapes is essential for the investigation of nanoscale structure-property relations. MPMN assembly has been studied via methods such as polymer-based molecular recognition⁹, hydrogen bonding¹⁰, and through the use of multidentate thioethers¹¹. The formation of MPMN aggregates using dithiol cross-linking¹² provides a reproducible method of spherical aggregate formation¹³. Now that a means for synthesizing aggregates has been developed, further application of the technology depends on practical examination of the environments in which the aggregates will be used.

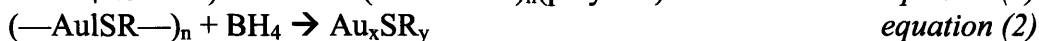
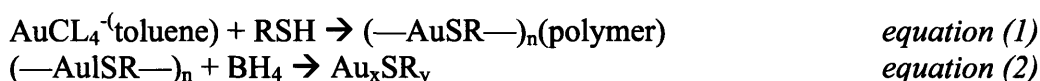
Bionanomaterials applications demand water-solubility of the nanoparticle aggregates in order to function within aqueous biological environments. Recent work has shown that Tiopronin and coenzyme-A can be used to induce solubility of MPMNs⁷ in water. The current study examines whether a simple place exchange reaction using a thiolated ligand with a polar end-group will produce water-solubility. Building on the reproducible Schiffrin method for MPMN formation, and the straightforward use of dithiols for aggregate formation, this work proposes an equally easy method for making water-soluble gold nanoparticle aggregates.

Chapter 2. Background Information

The keen interest surrounding nanoparticles in modern materials science stems from the unique size-dependent properties that they exhibit. With diameters of 1-10nm on average, these particles behave differently from both bulk and atomic-scale materials. Current applications for nanoparticles range from magnetic storage, disease therapy, photography, catalysis, and even cosmetics. Potential applications for this class of material are extremely broad, including such areas as novel nanoelectronic devices based on single electron tunneling through nanoparticle arrays. Gold and other coinage metals are often used in these applications due to the high reactivity of their surfaces, which can form stable bonds with passivating organic molecules, such as alkanethiols¹⁴.

A unique characteristic of nanoscale materials is the large percentage of their constituent atoms that are found at the surface. By altering the surface environment, one can see radical changes in the physical properties of the material. The formation of bonds between the surface atoms of gold nanoparticles and organic molecules lowers the free energy of the metal-environment interface. Through this thermodynamically driven process, SAMs form on the surface of gold nanoparticles. The SAMs used in the current study are made of thiolated ligands, each molecule possessing three basic components: a head group, showing a specific affinity for bonding to the surface, a carbon backbone, and an end group that determines the surface and interfacial characteristics of the nanoparticle. In addition to stabilizing the gold nanoparticles, the SAM lends its unique properties to the system⁵.

The basic method for formation of MPMNs via either one or two-phase synthesis was developed by Brust and Schiffrin in 1994. In the two-phase version, aqueous gold salt (AuCl_4) is combined with the phase transfer reagent, tetraoctylammonium bromide, in an organic solvent such as toluene. The thiolated ligands are added that will bond to the gold and form the SAM. Sodium borohydride (NaBH_4) functions as a reducing agent and the gold ions combine with the ligands in the organic phase. Equations 1 and 2 describe the reaction⁵.



The gold clusters grow until their surfaces are wholly covered in ligands. In practice, immersion time is inversely proportional to the concentration of the ligands in solution. Thus, the size of the gold clusters, as well as the time for SAM formation can be controlled using the ligand concentration³.

The Schiffrin model can be modified to create multi-ligand SAMs^{8,15}. Organization of the ligands into ordered domains can be induced by using ligands with hydrophobic and hydrophilic head groups, respectively. These “rippled” nanoparticles show ordered domains as small as 5Å , and demonstrate useful properties such as avoidance of non-specific adsorption of proteins⁶.

Rippled nanoparticles can be induced to form aggregates via a place-exchange reaction with a dithiol linker molecule¹³ [Figure 2]. The nanoparticles are combined with the dithiol molecules dissolved in a nonpolar solvent such as tetrahydrofuran (THF). In order to support ordered phase separation of ligand domains, defects exist at opposite poles, showing high reactivity. It is at these sites that the dithiol molecules place

exchange, linking the nanoparticles to form aggregates⁶. Evidence of aggregation can be seen from a redshift in optical absorption spectra, indicating the formation of nanoparticle aggregates.

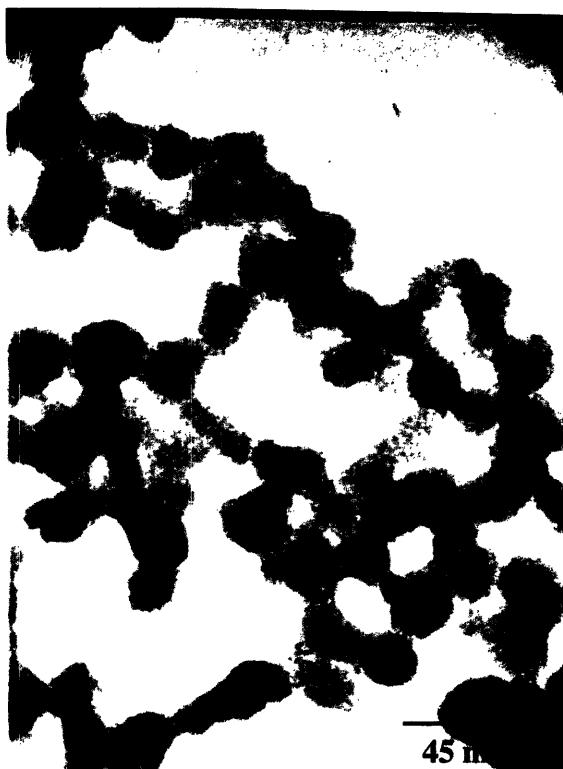


Figure 2. TEM image showing nanoparticle aggregates.

The nanoparticle aggregates formed via this process are readily soluble in nonpolar solvents, owing to the nature of the thiolated ligands; however, water-solubility is not originally achieved. Areas of research such as bionanotechnology would profit from water-soluble aggregates for drug delivery and contrast agents. Initial results of this study suggest that water-solubility can be achieved via a place exchange reaction between the rippled nanoparticle ligands and thiolated ligands with a polar head group.

Chapter 3. Experimental Methods

3.1 Materials

The chemicals used in the synthesis of gold nanoparticles were hydrogen tetrachloroaurate trihydrate, sodium borohydride, tetraoctylammonium bromide, and thiolated ligands (nonanethiol ($\text{CH}_3\text{-(CH}_2\text{)}_{10}\text{-SH}$, NT), methylbenzenethiol ($\text{CH}_3\text{-(C}_6\text{H}_4\text{)-SH}$, MBT)). Octanedithiol ($\text{SH-(CH}_2\text{)}_8\text{-SH}$, ODT) was used to form the nanoparticle aggregates. The solvents used in the nanoparticle synthesis, aggregate synthesis, sample preparations, and characterizations were toluene, methanol, tetrahydrofuran (THF), and chloroform. . All chemicals were purchased from Sigma-Aldrich and used as received. 11-mercapto-undecane-1-sodiumsulfonate (MUS) was synthesized in the laboratory.

3.2 Synthesis of Gold Nanoparticles

The gold nanoparticles were synthesized using Schiffrin's method of two-phase synthesis. 0.9mmol of hydrogen tetrachloroaurate (355 mg) were dissolved in 50 mL of deionized (DI) water, and the solution was stirred for ten minutes. 2mmol of the phase transfer reagent, tetraoctylammonium bromide (1903 mg), were added to toluene. After stirring for ten minutes, 0.6mmol of NT (113 mL) and 0.3mmol of MBT (35mL) were introduced, and the solution was stirred for a further ten minutes. A solution of 500mg of sodium borohydride in 50 mL of DI water was prepared and slowly added to the gold-thiol solution, a dark color resulting temporarily with each drop. After completion of the addition, the reaction was stirred for thirty minutes, followed by a phase separation in a separatory funnel. The clear aqueous phase was removed, and the toluene from the

organic phase was evaporated to eighty percent completion in a rotary evaporator. The remainder was diluted with 200 mL ethanol and stored overnight. The rippled nanoparticles formed a fluffy settlement at the bottom of the flask.

The contents of the nanoparticle solution were filtered using filter paper placed in a Büchner funnel. After wetting the filter paper with DI water, followed by ethanol, the solution was filtered under suction so that the supernatant passed quickly through the filter. Upon reaching the black nanoparticles at the bottom of the flask, filtering speed was decreased. After completion, the filter was carefully rinsed three times with ethanol, DI water, and acetone. The paper was dried thoroughly and the nanoparticles scraped off.

3.3 Synthesis of Gold Nanoparticle Aggregates

The nanoparticle aggregates were formed by adding dithiol solution to the rippled nanoparticles in THF. The dilute dithiol solution was prepared using 33.7 μ L of ODT in 10mL THF. 0.1mL of this dilute solution was combined with 4mg of nanoparticles in 1mL THF, and stirred for twenty minutes. 5-10 drops of the resulting solution was centrifuged in methanol, a “bad solvent.” This caused aggregates to precipitate, and the clear supernatant containing the excess thiol was removed. The centrifuging process was repeated for the entire solution, and the resulting nanoparticle aggregates were sonicated and redissolved in THF. In a temperature study of aggregate formation, the above procedure was carried out with the solution stirring in a vial within a beaker of water at 70°C.

3.4 Synthesis of Water-soluble Gold Nanoparticle Aggregates

In order to make the aggregates water-soluble, a place exchange reaction was carried out between the NT and MBT ligands and MUS, a thiolated ligand with a polar head group. The MUS solution was prepared using 5mg of MUS in 1mL of THF. Approximately five drops of DI water was added to this solution so that the MUS would be fully miscible in THF. 0.5mL of the MUS solution was combined with 1.5mg of nanoparticle aggregates in 1mL THF, and stirred for two days.

3.5 Characterization of Gold Nanoparticle Aggregates

The morphology of the nanoparticle aggregates was characterized using a tunneling electron microscope (TEM). The aggregates were prepared according to the method above. To obtain the TEM images, the nanoparticle aggregates were dropped on standard, 200-mesh carbon-coated copper TEM grids (LADD Research), and a JEOL 200CX tunneling electron microscope at 200kV. Images were captured using the digital image capture utility on the TEM.

The surface topology of the aggregates was studied using a Digital Instruments Nanoscope III Multiprobe atomic force microscope (AFM). AFM samples were prepared using a silica substrate cleaned with a highly reactive piranha solution ($H_2S_4:H_2O_2$, 3:1). Aggregate solution was then dropped onto the substrate and the solvent was allowed to evaporate before examination in the AFM.

3.6 Water-Solubility Testing of Gold Nanoparticle Aggregates

The water-solubility of the aggregates was tested by conducting the phase exchange reaction in a two-phase system. Nanoparticle aggregates (~1.5mg) in 1mL chloroform were combined with 2.5mg MUS in 0.5mL of DI water. The solution initially showed phase separation between the aqueous and chloroform phases, with the nanoparticle aggregates lending a dark color to the bottom, aqueous phase. The solution was stirred overnight.

Chapter 4. Results and Discussion

The aim of this study is a two-part investigation of the properties of gold nanoparticle aggregates. First, the dependence of morphology and size on formation temperature was examined. Second, using the room temperature aggregates, a place-exchange reaction was undertaken to induce water-solubility.

While the main goal of this study was to create water-solubility in the nanoparticle aggregates, a temperature study was undertaken on the aggregates themselves. By forming the aggregates at room temperature and 70°C, the effect of temperature on the size and morphology of the nanoparticle-dithiol aggregates was studied using AFM and TEM images, respectively. Changes in size and density indicated a phase change of the aggregates.

Water-soluble aggregates were fabricated by functionalization with MUS, a thiolated ligand with a polar head-group. The water-solubility of the aggregates was tested using a two-phase aqueous-nonpolar solvent experiment. Once the solubility of the aggregates was confirmed, the effect of the MUS place-exchange reaction on aggregate size was studied using TEM images.

4.1 Nanoparticle Aggregate Sizes Evaluated via AFM Imaging

AFM imaging was used to determine the average sizes of nanoparticle aggregates formed at room temperature and at 70°C. Two images were taken of both samples, and data were collected for height and width of the particles. Sizes were obtained in order to determine if any phase change occurred between the two temperatures. The average

height and width of the room temperature aggregates was approximately 70nm and 400nm, respectively. The samples formed at 70°C showed a larger average height of around 105nm, and a comparable width of around 350nm [Figure 3]. This increase in height for the 70°C aggregates could likely correspond to an increase in density of the aggregates. Such an increase in density would indicate a phase change in the aggregates, though the exact nature of such a phase change is not yet understood.

4.2 Nanoparticle Aggregate Sizes Evaluated via TEM Imaging

TEM imaging was used to determine the morphology of the room temperature and 70°C aggregates [Figure 4]. The 70°C aggregates had a darker appearance, compared to the room temperature aggregates, in which individual nanoparticles can be distinguished. This characteristic supports the argument for the existence of a phase change between room temperature and 70°C. Additionally, the aggregates formed at 70°C appear larger in the TEM images, although the AFM measurements indicated that only the vertical dimension increased between room temperature and 70°C. Overall, it appears that the 70°C aggregates were larger and denser than those formed at room temperature.

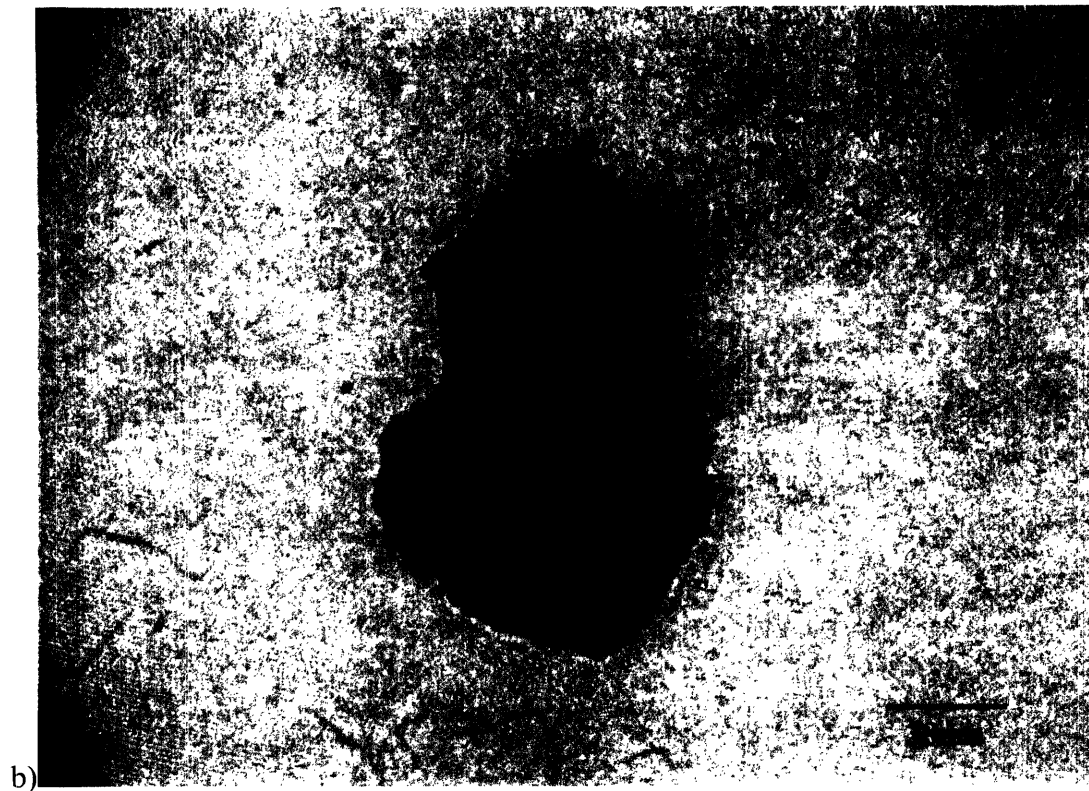
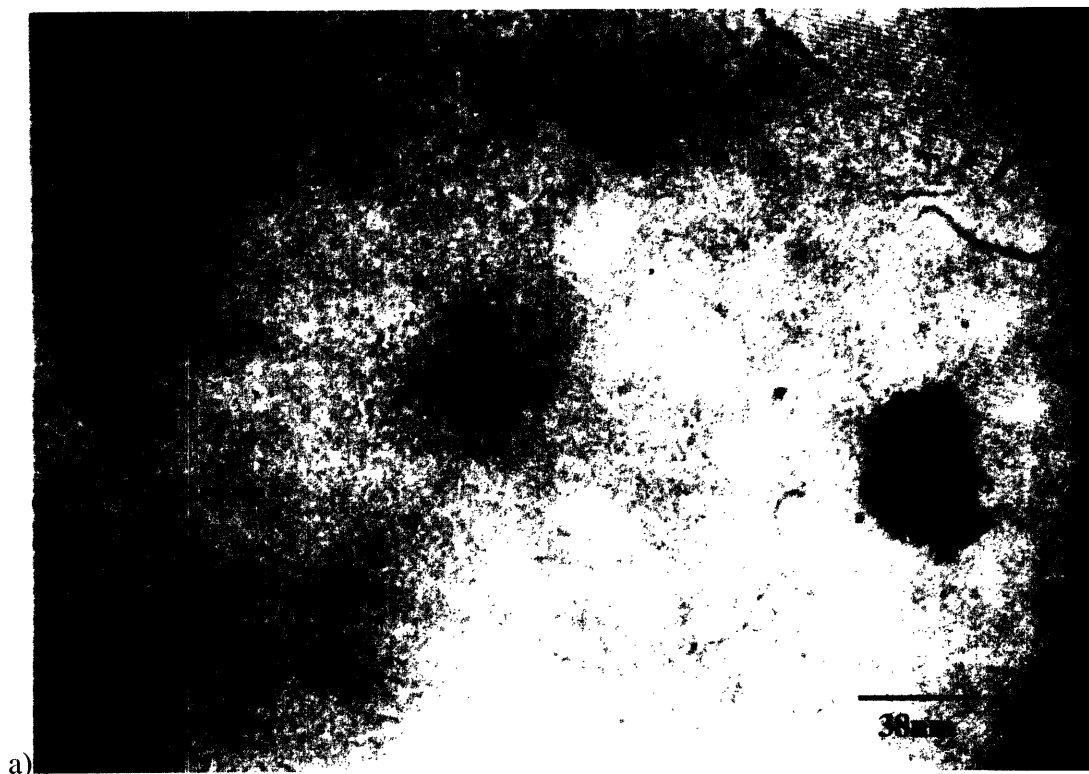


Figure 4. a) TEM image of aggregates formed at room temperature (27K magnification),
b) TEM image of aggregates formed at 70°C (27K magnification)

4.3 Water-Solubility of MUS-Functionalized Nanoparticle Aggregates

The Water-Solubility of the MUS-functionalized aggregates was demonstrated using the two-phase chloroform/water experiment described. After stirring overnight, the aggregates transferred into the aqueous phase, as shown by a change in color of the water phase from clear to dark [Figure 5]. The aggregates remained in the aqueous phase for at least three weeks, up to and including the writing of this report.

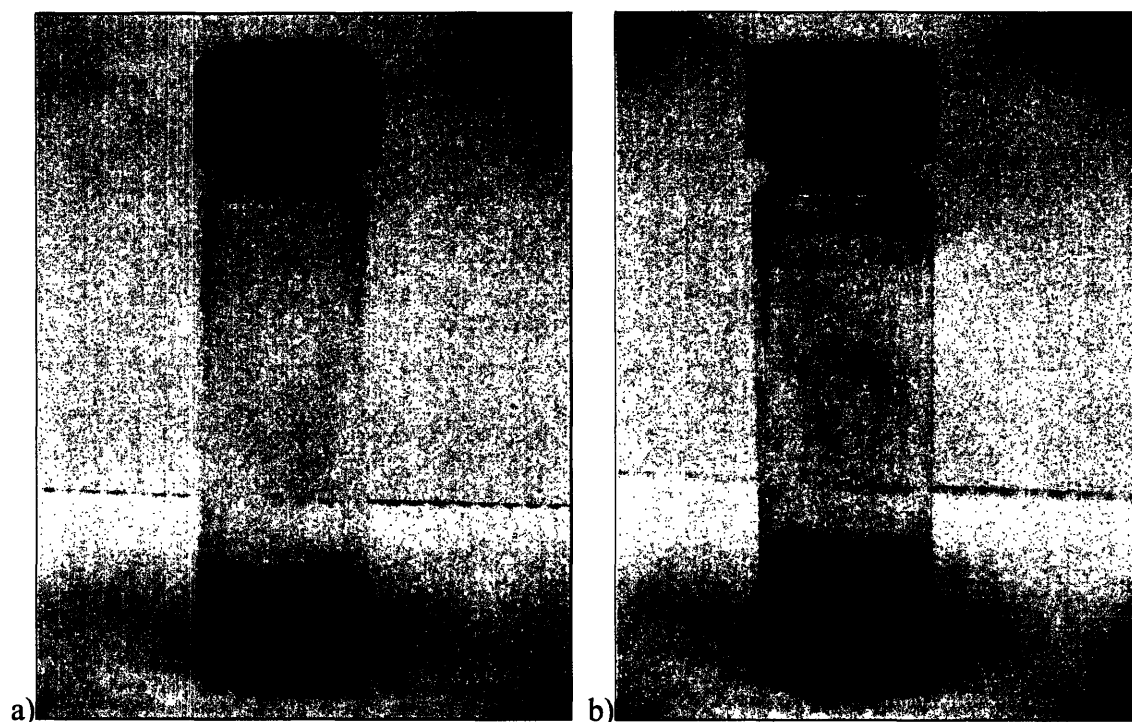


Figure 5. a) Photograph of two-phase aqueous/chloroform system, before stirring, showing the nanoparticles in the chloroform phase, b) Photograph of two-phase aqueous/chloroform system, after stirring, showing the nanoparticle aggregates transferred to the upper aqueous phase.

4.4 Water-soluble Nanoparticle Aggregate Sizes Evaluated via TEM Imaging

TEM imaging was used to find the size and morphology of water soluble aggregates compared to room temperature aggregates [Figure 6]. The average size for water-soluble aggregates was 75nm, compared to 55nm for room temperature aggregates.

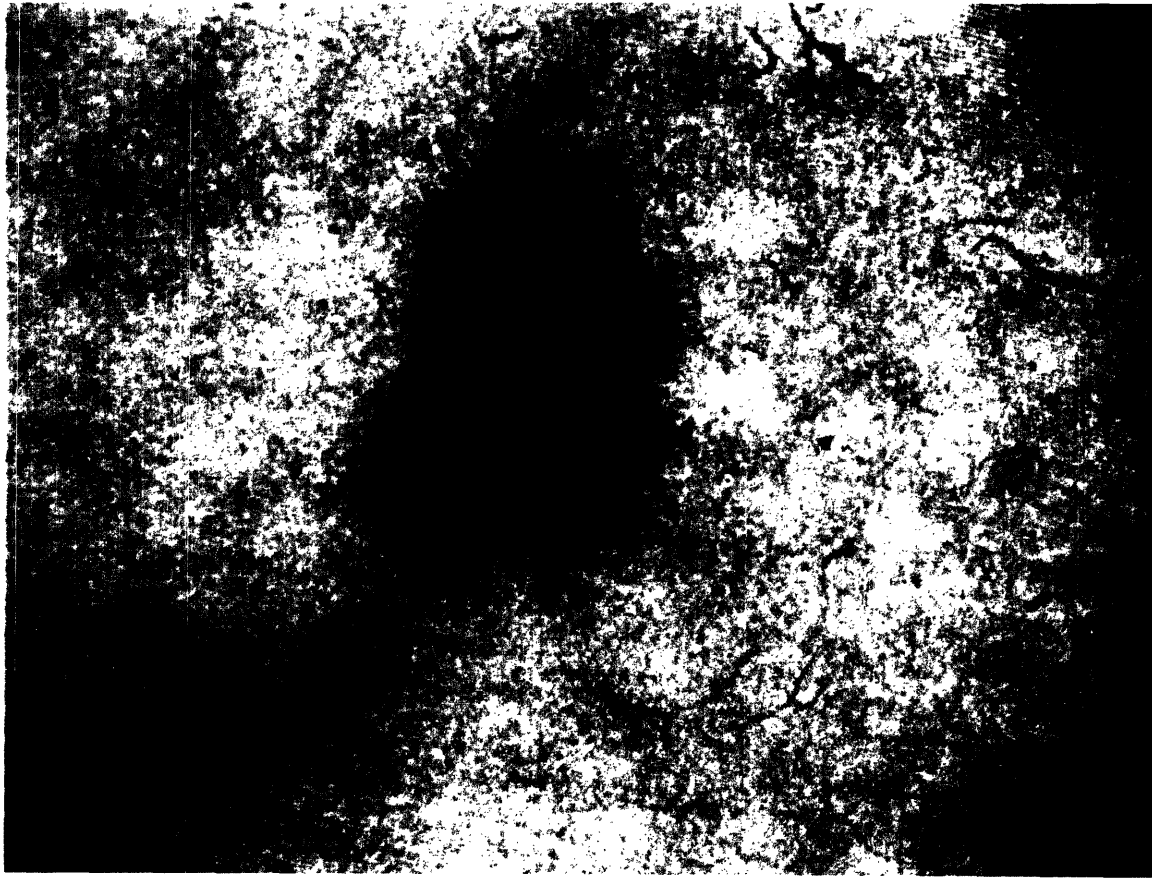


Figure 6. TEM image of water-soluble aggregates (27K magnification)

Chapter 5. Conclusions and Future Work

The behavior of monolayer-protected metal nanoparticles and the systems that they can form present a new and exciting area of research. In this study, we demonstrated a likely phase transition of the aggregates between room temperature and 70°C. Both AFM and TEM imaging indicated that the aggregate size increased in the aggregates formed at high temperature. Additionally, the TEM images showed a denser morphology for the 70°C aggregates.

The aggregates were functionalized with MUS via a place-exchange reaction in order to induce water-solubility. These aggregates showed stability in aqueous phase, indicating that the MUS reaction was successful. Upon realization of water-solubility, the aggregates can be used in biological systems or other aqueous environments. The TEM images showed similar morphology to the room temperature samples; however, the size of the water-soluble aggregates increased slightly. The statistical significance of this increase should be the subject of further investigation.

Further study should more thoroughly investigate the temperature-induced phase change of the nanoparticle aggregates. Effort should be made to determine if the phase change is dependant upon formation at high temperature, or if aggregates formed at room temperature can be heated and induced thereby to undergo phase transformation. Additionally, the transformation should be investigated to determine the exact temperature of transition and any inter-phase transitional properties of the aggregates.

The study of water-solubility can be expanded to investigate the effect of concentration of polar thiolated ligand on the solubility. A minimum concentration of

polar ligand necessary to induce solubility should be found, as well as any possible effects of excess presence of polar ligands in the reaction. Alternative polar ligands to MUS can be considered, varying the length of the thiol, as well as the nature of the head group.

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