Stabilization of Gold Nanoparticles by 6-Mercaptopurine Monolayers. Effects of the Solvent Properties

Alfonso J. Viudez, Rafael Madueño, Teresa Pineda, and Manuel Blázquez*

Departamento de Química Física y Termodinámica Aplicada, Universidad de Córdoba, Campus de Rabanales, Ed. Marie Curie, E-14071 Córdoba, Spain

6-Mercaptopurine-coated gold nanoparticles (6MP−AuNPs) have been prepared by modification of the nanoparticle surface with 6MP upon displacement of the protective layer of citrate anions. The modification has been studied by UV−vis and FTIR spectroscopies. A study of the stability of these 6MP−AuNPs in aqueous solutions as a function of ionic strength and pH has shown the importance of the charges on the stabilization. The protonation of N9 of the 6MP molecules brings about a sudden flocculation phenomenon. However, the flocculation is reversible upon changing the pH to values where the molecules become newly charged. Evidence of the competence between the interaction of capping solvent molecules and the attractive forces between particles is also shown in this paper.

Introduction

Metal particles in the nanometer size range have gained considerable interest in recent years.[1−3] The simplest and the most commonly used bulk-solution synthetic method for metal nanoparticles is the chemical reduction of metal salts. The particle synthesis usually makes use of a soluble metal salt, a reducing agent, and a stabilizing agent. The stabilizing agent caps the particle and prevents further growth or aggregation. Reducing agents such as citrate[3−5] and sodium borohydride[5−7] are commonly used for the preparation of metal nanoparticles. Polymers and organic molecules bind to the particle surface and thus serve the role of a stabilizer.

Surface functionalization of metal nanoparticles can be performed by using two basic approaches. One is performing the surface modification of colloidal gold preparations by chemisorption of thiol derivatives, and the other implies the synthesis of thiol-modified colloidal metals in a one-step procedure. The latter is based on modifications to the synthetic procedure originally reported by Brust to create metallic nanoparticles.[8,9] Brust synthesis consists of reducing a metallic salt (AuCl₄H) in the presence of alkanethiol and results in nanoparticles protected by an organic monolayer which are called monolayer-protected clusters (MPCs). Such a monolayer confers these systems with new surface properties and also with extraordinary stability so that they can be isolated and manipulated with a variety of chemical and physical procedures to the extent that they can be dried and resuspended in solution again without suffering irreversible aggregation or decomposition.[10−15]

In general, the synthesis of MPCs yields polydisperse size distributions of nanoparticles of sizes under 10 nm.[11−15] For some applications, it may be desirable to obtain functionalized gold nanoparticles of sizes larger than those of the MPCs and with monodispersed sizes. In fact, the optical sensing of the nanoparticles relies on the chromophoric characteristics whose molar extinction coefficient of the surface plasmon band is proportional to the particle volume.[16,17] A satisfactory sensitivity

would demand a larger particle size than the MPCs have and thus require another synthetic strategy.

Alternatively, gold nanoparticles bearing both excellent optical sensitivity and excellent stability can be obtained by the synthesis of nanoparticles of a certain size,[3,18] followed by surface modification by thiol derivative chemisorption on the spheres of the colloidal gold.

The combination of the unique surface plasmon resonance property of gold nanoparticles and the strong affinity of thiol to gold serves as a good strategy to obtain nanoparticles of the desired properties.

When the gold nanoparticles are exposed to a solution of thiols, the interaction of these molecules with the gold surface takes place. To chemisorb, the thiols must displace the anions (normally citrate anions) that act as protector agents of the gold colloid. Thus, desorption of charged species sacrifices the electrostatic stability and sometimes causes irreversible aggregation.[19−23] The modification of gold nanoparticles with ω-functionalized thiol in aqueous solution can cause irreversible aggregation when the thiol is not negatively charged. This fact is evidenced by the color change to blue accompanied by a red shift of the surface plasmon bands.[17,19] TEM images of these systems reveal the fusion of gold cores,[20,21] allowing us to think that during the displacement of the adsorbed anions by the thiol derivative the electrostatic stability is lost. In fact, the problem arises because it is very difficult to simultaneously preserve the charges and assemble the protective monolayer.

Recent studies in our laboratory have demonstrated the ability of 6-mercaptopurine (6MP) (Chart 1) to form compact and stable monolayers on gold surfaces of different orientations.[24−26] The use of gold substrates of different arrangements at the atomic level is of great interest not only because it allows new structural aspects to be observed but also because it presents the opportunity to find new chemical properties of the self-assembled monolayers (SAMs). In this sense, the modification of gold nanoparticles (AuNPs) with different SAMs is interesting on one hand for the different sizes they present depending on the method of synthesis chosen and, on the other hand, for the overall geometric shape that makes the surface have a high

* To whom correspondence should be addressed. Phone: +34-957-218646. Fax: +34-957-218618. E-mail: qf1blrum@uco.es.

6-Mercaptopurine-Modified Gold Nanoparticles

J. Phys. Chem. B, Vol. 110, No. 36, 2006 **17841**

CHART 1
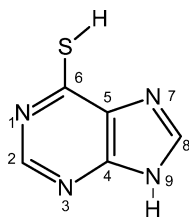
radius of curvature that allows these systems to be thought of as three-dimensional monolayers (3D-SAMs).[27] In the present work, the modification of a gold colloid (AuNPs) by 6MP is carried out. The characterization of the 6MP−AuNPs is accomplished by UV−vis and IR spectroscopies and transmission electronic microscopy techniques.

The modification of the AuNPs by 6MP occurs by a very fast reaction that allows the stabilization of the 6MP−AuNPs. The 6MP−AuNPs are stable in a wide range of experimental conditions in an aqueous medium. In an acidic medium, the 6MP−AuNPs flocculate, but this process is reversible as a stable suspension is obtained when the pH of the medium is changed.

Experimental Section

All chemicals were reagent grade and used as received. Milli-Q water was used to prepare the solutions. All glassware was thoroughly cleaned with aqua regia and rinsed with Milli-Q water prior to use.

The synthesis of AuNPs was carried out by following the classic method of Turkevitch et al.[5] and improved by French[18] that consists of the reduction of $HAuCl_4$ by citrate anions in an aqueous medium. The citrate anions not only serve as a reductor agent but also exert a protection effect against the aggregation of the particles synthesized. Briefly, the gold nanoparticles were prepared as follows.[28] In a 1 L Erlenmeyer flask, 500 mL of 1 mM $HAuCl_4$ was brought to a boil, with vigorous stirring on a magnetic stirring hot plate. A 50 mL sample of 38.8 mM sodium citrate was added to the solution all at once, with vigorous stirring. The yellow solution turned clear, dark blue, and then a deep red-burgundy color within a few minutes. Stirring and boiling was continued for 10−15 min after the burgundy color was observed. The solution was then removed from the heat and stirring continued for 15 min. After the Au colloid solution had cooled, the volume was adjusted to 500 mL with H_2O. Considerable volume loss (due to evaporation) can occur during the preparation; this can be avoided if the synthesis is performed under refluxing conditions. The solution was stored in a clean brown glass bottle until use (the shelf life is from several weeks to months).

The average diameter measured by TEM (Philips CM-10 and JEOL JEM 2010 instruments) was 13 nm with Image-Pro Plus software.

The pH measurements and the acid−base titration were made with a Crison Basic 20 pH meter.

UV−vis spectra were recorded with a Perkin-Elmer Lambda 3 spectrometer with 1 cm path length cuvettes. Transmission FTIR spectra were recorded with an FTIR Mattson, Research Series, spectometer that uses a DTGS detector.

Results and Discussion

Modification of AuNPs by 6MP. The modification of the AuNPs was carried out by adding an excess of 6MP to the AuNP aqueous solutions. Under these experimental conditions, only a slight change in the surface plasmon resonance (SPR) band
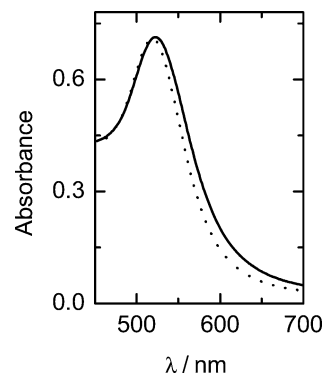

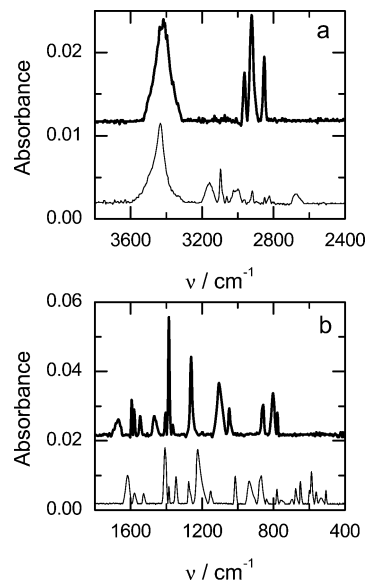**Figure 1.** UV−vis spectra of AuNPs (···) and 6MP−AuNPs (—) in water (pH 7).

Figure 2. Transmission FTIR spectra of pressed KBr pellets containing free 6MP (thin solid line) and 6MP−AuNPs (thick solid line).

is observed. In Figure 1 the spectra of the 6MP−AuNPs together with that registered before the addition of 6MP are shown. A small displacement (∼3 nm) of the SPR band maximum due to the presence of the 6MP monolayer built on the particle surface is observed. This effect has also been observed upon surface modification of gold nanoparticles of different sizes and explained on the basis of changes in the dielectric constant in the immediate layer to the gold core.[10,16]

To prove that a 6MP−SAM has been formed on the gold nanoparticle surface, a study by FTIR spectroscopy has been carried out. The sample of 6MP−AuNPs was first dialyzed against an aqueous solution to remove the 6MP molecules that have not reacted with the AuNPs. In the second step, the suspension was centrifuged and the precipitate was separated from the supernatant and dried in a vacuum at room temperature. The solid 6MP−AuNPs were mixed with KBr, and a pellet was formed. The IR spectrum obtained for the 6MP−AuNPs is plotted in Figure 2 together with that for the free 6MP taken under the same experimental conditions. The analysis of the spectra has been made with reference to the theoretical assignation of the IR bands reported in the literature for the 6MP molecule.[29]

The band at 3433 cm^{-1} in the higher frequency region (Figure 2a) is assigned to the N−H stretching modes. The 6MP molecule exists as different main tautomeric forms: the N(9)−H and N(7)−H thiol and the N(1)−H, N(9)−H and the N(1)−H, N(7)−H thione tautomers (Chart 2). Thus, the band should

CHART 2

| thiol N(9)-H | thiol N(7)-H | thione N(9)-H | thione N(7)-H |
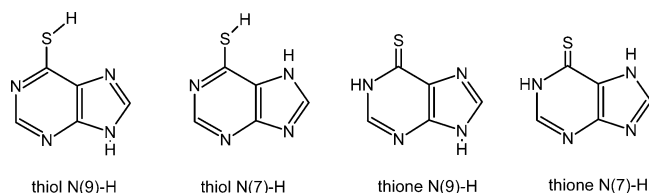
contain the contribution of the corresponding N−H stretching modes. In fact, a mixture of tautomers is thought to exist under the conditions of the experiment involving the 6MP molecules.[29−32]

In the 3200−2700 cm^{-1} region, several bands at 3158, 3095, 3006, 2966, 2924, and 2853 cm^{-1} are assigned to the C(8)−H and C(2)−H stretching modes on the different tautomers. Moreover, a band at 2671 cm^{-1} due to the S−H stretching vibration is found. This band is of a lower intensity but always appears in the free 6MP spectra. Then, in agreement with the presence of these bands in this spectral region, it can be concluded that thiol species exist in the sample, although the presence of thione species should also be taken into account. Upon modification, the band at 2761 cm^{-1} disappears, proving that 6MP is bound to the Au surface by the 6-SH group. On the other hand, several stretching C−H bands in the 3200−3000 cm^{-1} disappear, and three bands at 2966, 2924, and 2853 cm^{-1} increase in intensity. The increased intensities can be due to the transformation of the different tautomers existent in the free molecule to the thiol species in the adsorbed state. The formation of SAMs might naturally tend to select a conformation of molecules with the lowest minimized energy. This effect has been observed in the 6MP−SAM formed on gold by using SERS,[31,32] where the molecules adopt the thiol form.

The region of 1800−400 cm^{-1} is more complex. However, some details that could be distinguished are going to be highlighted. In the spectrum of free 6MP, two pair of bands at 505 and 561 cm^{-1} and 533 and 584 cm^{-1} that correspond to the bending modes of the N(9)−H bond in the thiol N(9)−H or to the N(7)−H bond in the N(1)−H, N(7)−H thione species, respectively, are observed. Moreover, these bands have some contribution of the C−S bending mode. Other bands at 644, 675, 695, and 757 cm^{-1} that correspond to ring vibration modes disappear when 6MP binds to the gold surface as also occurs with the N−H bending bands mentioned above. The disappearance of these bands in the spectrum of 6MP−AuNPs can be explained by the preference of all the adsorbed 6MP molecules for a specific tautomer conformation. However, this fact cannot account for the complete elimination of the signals down to 750 cm^{-1}. The surface selection rule for SAMs on planar gold substrates has been shown not applicable in the case of metal nanoparticles;[33] therefore, an explanation in terms of molecular orientation cannot be made. Another factor to bring about is the influence of the base stacking interactions that should operate in the adsorbed 6MP molecules on the IR bands, but this assessment needs further investigation.

The bands at 937 and 1013 cm^{-1} in the spectrum of free 6MP, which correspond to C(2)−H bending and other modes that include C−S stretching, S−H deformation, etc., increase in frequency upon binding to gold. A shift in the C−S vibration to higher frequencies would indicate an increase in the bond strength. This could happen if the thiol group binds to gold and loses the H atom. Then, the π-bond order of the C−S bond increases and gives place to the change observed. A similar effect has been found in the SERS spectra of 6MP−Ag.[34]

The three bands at 1527, 1578, and 1615 cm^{-1} are maintained

in the 6MP−AuNP spectrum although some changes in frequency are obtained. These changes are in agreement with the implication of the two rings of the 6MP molecules in the interaction with gold. The important change from 1615 to 1667 cm^{-1} upon binding to gold implicates an important change in the C(5)−N(7) stretching of the thiol species. The higher frequency of the C−N stretching would indicate a higher strength of the C(5)−N(7) and C(8)−N(7) bonds that could originate in the interaction with Au, which should donate the electronic density that accounts for that increase.

Stability of 6MP−AuNPs in Aqueous Solutions. The stability of colloidal dispersions can be evaluated by changes in their optical spectra. Qualitatively, flocculation is reflected by a change in color from red to violet or blue, followed by precipitation of colloids from the solution. To avoid flocculation, the nanoparticles need a small surface charge. This charge is provided by the adsorbed citrate anions and, upon surface modification by an organic molecule such as 6MP, is neutralized. If the neutralization is not complete, the small surface charge on each nanoparticle makes them repel from each other, and the result is the formation of long chainlike aggregates as opposed to the dense clusters that are observed when the surface charge is completely lost.[35]

Chen et al.[23] have proposed a two-step functionalization of neutral and positively charged thiols onto citrate-stabilized gold nanoparticles. The anions are first displaced by thioctic acid, which is then exchanged by thiols containing the desired functionality during the second step. They explain the stability of thioctic acid-modified gold nanoparticles as a result of charge preservation upon displacement of the adsorbed citrate anions by the negatively charged thiols. On the other hand, Perez-Luna et al.[22] have developed a strategy to sterically protect gold nanoparticles by using a nonionic surfactant, Tween 20, prior to the nanoparticle modification with carboxylate-terminated alkanethiols, thus preventing the nanoparticles from aggregating in the subsequent reaction.

To avoid the formation of aggregates, the modification of AuNPs by 6MP in an alkaline medium has been carried out. Under these conditions, the 6MP molecules are negatively charged[36,37] and maintain the charge on the surface. The 6MP−AuNPs formed under these conditions are stable even after the citrate anions are removed by dialysis. Moreover, they can be precipitated by centrifugation, and the pellet obtained can be redissolved without any signal of aggregation. The high stability of the 6MP−AuNPs comes from the fast citrate anion displacement reaction by the 6MP molecules that avoid partial neutralization of the surface charge.

The spectral changes accompanying flocculation of gold colloids have been extensively studied. The visible extinction (absorption of light plus scattering) in dispersions of nearly spherical metal colloids was first theoretically interpreted by Mie,[38] who showed that a metal sphere whose radius is much smaller than the wavelength of light will absorb a certain wavelength by resonant excitation of surface plasmons. For spherical gold colloids dispersed in water, this excitation occurs at approximately 520 nm. In general, the excitation wavelength depends on the radius of the sphere and the dielectric constant of both the metal and the medium in which it is dispersed.[39] If the metal particle is elongated in one or two dimensions to make it highly anisometric, red-shifting and broadening of the extinction spectrum results.[40]

The flocculation of individual spheres also results in red-shifting and broadening in the visible spectrum.[41] In this sense, when the distance between flocculating spheres is small
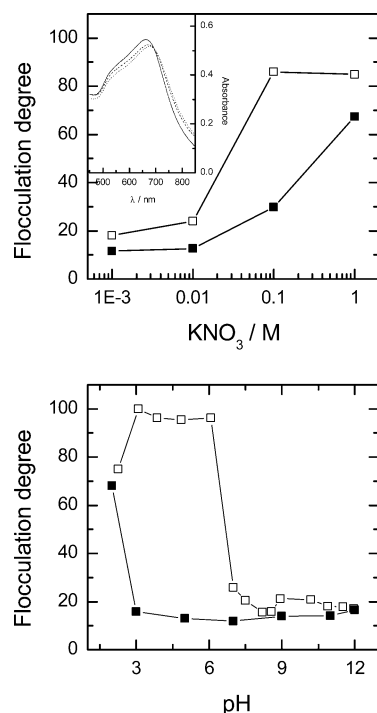
6-Mercaptopurine-Modified Gold Nanoparticles

J. Phys. Chem. B, Vol. 110, No. 36, 2006 **17843**

Figure 3. Flocculation of AuNPs (■) and 6MP−AuNPs (□) as a function of (a) KNO_3 concentration and (b) pH. Dispersions are pipetted into aqueous solutions that contain varying concentrations of KNO_3 at pH 7 (a) or aqueous solutions at different pH values. Inset: UV−vis spectra of 6MP−AuNPs after 1 min (—), 10 min (---), and 30 min (···) of the 6MP−AuNPs in 0.1 M KNO_3. The concentration of 6MP−AuNPs in the cuvette was estimated to be 3 nM.

compared to the radius of the spheres, additional resonances will occur at wavelengths that are longer than that of the resonance of the isolated sphere. These resonances are concentrated above 600 nm in the visible spectrum.

Whitesides et al.[19] use the term "flocculation" generically to describe the instability of colloids, as a clear distinction between aggregation (close, irreversible association) and agglomeration (loose, reversible association) of particles cannot be made spectroscopically. They used the integrated extinction between 600 and 800 nm as a quantitative measurement of the extent of flocculation of the particles.[19] In this work, we use the modified parameter obtained by subtraction of the area under the curve of the optical absorption spectrum of the uncapped gold sol from the actual area, once they have been normalized to the intensity at the surface plasmon resonance in the absence of flocculation.[42]

The synthesis of AuNPs is carried out in the presence of citrate anions that act not only as reductors but also as capping or protecting agents. The protection takes place through the adsorption of anions on the gold surface, and its stabilization has been discussed in terms of the DLVO theory as due to the electrostatic repulsion between the negative charged AuNPs. Then, the stability of AuNPs is strongly dependent on the ionic strength, the flocculation being produced above $\mu = 0.1$, at pH 7 (Figure 3). The kinetics of this process is very fast and is almost completed in the first minute after the salt addition. Such behavior is typical of colloids that are stabilized by charged double-layer repulsion,[43,44] where an increase of the ion concentration in solution should screen the interparticle electrostatic repulsion, and the AuNPs start to flocculate. Experiments carried out with the 6MP−AuNPs show that the flocculation parameter reaches the maximum value when the ionic strength is 0.1; that is, the stability is slightly lower than that of the AuNPs (Figure 3). The flocculation is slow in the

SCHEME 1
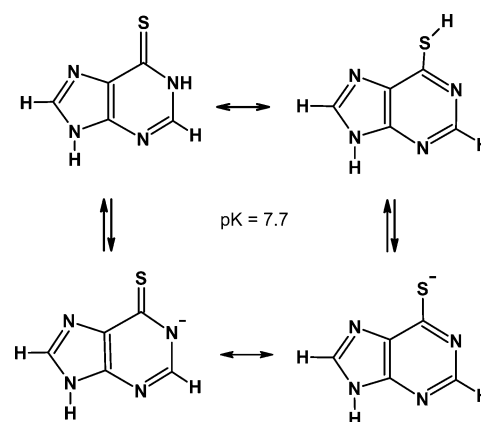
case of low ionic strength, but for higher salt concentrations the displacement of the absorption band is almost complete after 1 min (Figure 3, inset). However, after some time, the band remains unchanged and no precipitation takes place, suggesting that the aggregate size should not increase with time.

Moreover, under conditions of low ionic strength, the AuNPs remain stable in a wide pH interval: 3 < pH < 12. The dissociation equilibrium of the citrate (pK values are 3.28, 4.76, and 6.4[45]) can be responsible for the stabilization of the AuNPs in such a wide pH interval. The effect of pH is also different for the 6MP−AuNPs compared to the AuNPs (Figure 3). The onset of flocculation occurs at pH 7. To explain this behavior, a look at the acid−base properties of the free 6MP molecules is necessary. The 6MP molecule presents a highly complex acid−base behavior that is additionally complicated by the existence of different tautomeric species in solution. Scheme 1 represents the equilibrium[37] that is important to form the 6MP−Au interaction, that is, the SAM.

On the other hand, the 6MP molecule can be protonated at the N(1) position in a strong acidic medium, and the proton dissociation at the N(9)−H position takes place in an alkaline medium (p$K = 10.84$[46] or 11.17[36]). Thus, the formation of a SAM on Au takes place through reactions 1 and 2, in acidic and basic media, respectively.

$$R-SH + Au \rightarrow R-S-Au + H^+ \qquad (1)$$

$$R-S^- + Au \rightarrow R-S-Au \qquad (2)$$
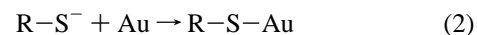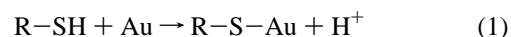
However, the state of the 6MP molecules when adsorbed to the Au surface is unknown at the moment. As occurs in the formation of SAMs of alkanethiols, the negative charge of the thiolate is transferred to the gold in the first step and later dissipated by a mechanism that is under discussion.[47,48] Under these conditions the Au−6MP SAM should be uncharged in the pH interval from the first pK (corresponding to the N(1) at pH < 3) up to pH ≈ 11, where the N(9)−H group dissociates and becomes negatively charged.

The sudden flocculation of 6MP−AuNPs that takes place at pH < 6 should be related to a change in the charge state of the monolayer. In fact, an acid−base titration of the 6MP−AuNPs (Figure 4) allows us to distinguish the existence of an apparent pK near pH 6. Then, taking the flocculation and the titration data together, it can be said that the 6MP molecules undergo a change in the overall charge state in this pH interval. It is possible that the dissociation of the N(9)−H group that takes place at pH 10.84−11.17 in solution causes a change to lower pH values upon adsorption of the molecules to the AuNPs. In
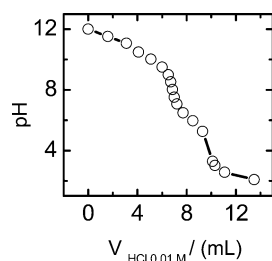
17844 *J. Phys. Chem. B, Vol. 110, No. 36, 2006*

Viudez et al.

Figure 4. Titration curve of 6MP−AuNPs. Titration was performed by adding 0.1−0.5 mL aliquots of 10 mM HCl to 1 mM 6MP−AuNP solutions in 10 mL of NaOH (0.01 M). The pH was recorded initially and after each addition of HCl solution.
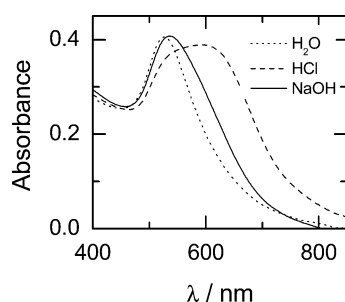

Figure 5. UV−vis spectra of 6MP−AuNPs in aqueous solution at pH 7 (···) and pH 3 (---). The spectrum given by the solid line corresponds to that shown at pH 3 after being changed to pH 7 by the addition of an aliquot of diluted NaOH solution.

this way, at pH < 6, the 6MP−AuNPs become neutral and the flocculation starts.

Changes in the surface pK values of ω-carboxylalkanethiols on gold with respect to free alkanoic acids in solution have been reported.[49] These increased values of the apparent pK of the SAMs have been explained as due to the repulsive interaction between the deprotonated groups, hydrogen bonding, the lower dielectric constant in the inner part of the double layer, and the imaging effect. The lateral attractive interaction caused by the van der Waals force would counteract the electrostatic repulsion after the deprotonation, but this effect should not be important as the observed trend in SAMs of ω-carboxylalkanethiol of different chain lengths is the opposite. However, there is agreement between the decrease in the dielectric constant of the inner part of the double layer and the shift in pK as this magnitude decreases.

In contrast, in the case of 6MP−AuNPs, the charged state of the molecules is favored with respect to the neutral state. This should mean that the intermolecular interactions (base stacking interactions) are very strong and compensate the electrostatic repulsion within the monolayer in a wide pH range. On the other hand, these interactions can increase the acidity of N(9), and therefore, a decrease of the pK for the adsorbed state can be produced in a way similar to that which has been reported for purine derivatives,[50] where the hydrogen-bonding interactions produce such an effect.

An interesting point is that the flocculation of 6MP−AuNPs is reverted when the acidity conditions in the solution change. Then, as can be observed in Figure 5, the absorption spectrum of the plasmon resonance band for the stabilized 6MP−AuNPs is almost recovered by the addition of NaOH to the previously acidified solution. This is evidence of the reversibility of the flocculation process in 6MP−AuNPs, which is differentiated from the behavior of the AuNPs, where it can be seen that, once the particles have interacted, they do not revert to the initial state. Thus, the 6MP monolayer exerts a protection effect against irreversible aggregation. In the terminology put forward by
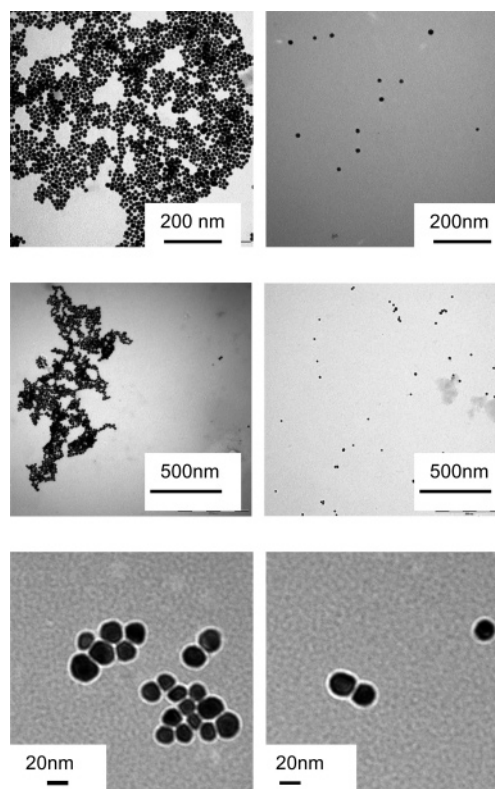

Figure 6. Representative TEM micrographs of AuNPs (top) and 6MP−AuNPs (middle and bottom) at pH 3 (left) and pH 7 (right).

Whitesides et al.[19] the phenomenon observed would be described as agglomeration. Such a reversible coagulation of metal colloidal particles with solution pH has been reported for silver colloidal particles derivatized using 4-carboxythiophenol[51] and for gold sols stabilized with sodium 3-thiopropionate.[52]

TEM images of the gold nanoparticles in acidic and alkaline media help to understand this behavior. The images in the acidic medium show that the particles form aggregates, whereas in the alkaline medium they stay well separated. Moreover, in a high-resolution image, it can be observed that even in an acidic medium the 6MP−AuNPs do not fuse their cores, showing a separation layer that approximately amounts to two monolayers of 6MP (Figure 6).

Effect of Organic Solvents on the Stability of 6MP−AuNPs. Underwood and Mulvaney[39] have shown that the color of the polymer-stabilized gold sol is in agreement with the Mie theory. They observed a shift in the surface plasmon absorption of gold nanoparticles when the solvent refractive index was varied that obeys eq 3,[16] where λ_p is the bulk plasma wavelength, ϵ_∞ is the high-frequency dielectric constant due to interband and core transitions, and ϵ_m is the medium dielectric constant.

$$\lambda^2 = \lambda_p^2(\epsilon_\infty + 2\epsilon_m) \tag{3}$$

Mulvaney et al.[10] found a change in the plasmon band position of dodecanethiolate MPCs that agreed well with the predictions of the Mie theory when the alkanethiolate monolayer was accounted for in the calculation. The effect of the ligand chain length on the SPR band of gold colloids can be accounted for by considering the contribution of the dielectric constant of the organic shell. When a metallic nanoparticle is induced by a ligand shell whose refractive index is different from that of the ambient (i.e., a gold nanocore), the field that acts on the particle is no longer homogeneous. The dense shell of binding ligands provides a dielectric coating on the particle surface, amounting
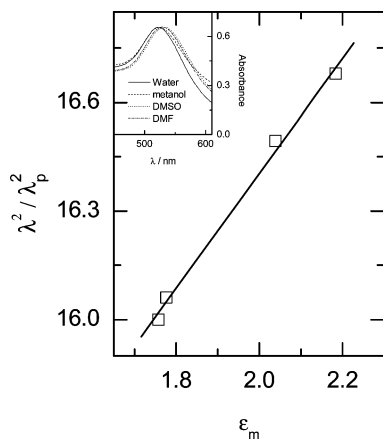
6-Mercaptopurine-Modified Gold Nanoparticles

J. Phys. Chem. B, Vol. 110, No. 36, 2006 **17845**

Figure 7. Effects of changes in the refractive index on the SPR band properties of 6MP−AuNPs. Inset: UV−vis spectra of 6MP−AuNPs in different solvents. The dispersion of 6MP−AuNPs in a water solution was centrifuged for 15 min at 15000 rpm, and the precipitate was redispersed in different organic solvents.

Figure 8. Effect of the variation of the solvent dielectric constant on the flocculation degree of 6MP−AuNPs. Inset: UV−vis spectra of 6MP−AuNPs in different solvents: (1) water; (2) ethylene glycol; (3) acetone; (4) propanol; (5) 2-propanol; (6) dioxane. The dispersion of 6MP−AuNPs in a water solution was centrifuged for 15 min at 15000 rpm, and the precipitate was redispersed in different organic solvents.

to a change in the dielectric constant of the medium and causing a red shift of the λ_{max} of the SPR band. In a system of metal particles where the combination of solvent and ligand shell is very similar in terms of refractive index, the particles may be treated as if they are in a homogeneous solvent. However, if there is a difference in the refractive index value, the field around the particles is not homogeneous anymore. Mulvaney et al.[10] thus modified eq 3 by including the contribution of the dielectric constant of the organic shell to give a more accurate description of the surface plasmon peak position (λ) as

$$\lambda^2 = \lambda_p^2[(\epsilon_\infty + 2\epsilon_m) - 2g(\epsilon_m - \epsilon_s)/3] \quad (4)$$

where ϵ_s is the dielectric function of the shell layer (assuming that the medium is nonabsorbing, ϵ_s is the dispersionless optical dielectric function of the shell and is related to the refractive index of the shell layer by the relation $\epsilon_s = n_s^2$) and g is the volume fraction of the shell layer, which increases with the chain length of the organic capping agent:

$$g = \frac{[(R_{core} + R_{shell})^3 - R_{core}^3]}{(R_{core} + R_{shell})^3} \quad (5)$$

Pal et al.[53] studied the optical properties of surfactant-stabilized gold nanoparticles in a variety of organic solvent systems without any aggregation. They found that the interaction of the solvents with the gold particles follows two different trends. In some cases, the variation of the λ_{max} of the SPR band is linearly dependent on the refractive index of the solvent (n_s), whereas, in some other cases, a nonlinear variation is observed. They explain this behavior as the solvents that do not possess any active functional groups and remain inert, with no noticeable chemical interactions with the gold surfaces, gradually shift the maximum wavelength toward the red with an increase in the solvent refractive index. On the other hand, the polar solvents are capable of complexing with gold surfaces through direct charge-transfer interaction, and they have different extents of electron injection capabilities. In an earlier study, Thomas et al.[54] found a similar behavior for the TOAB-capped gold particles in different organic solvents, but they explain the lack of agreement with eq 3 or eq 4 with polar solvents as due to the complexation of the solvent molecules that penetrate the shell and alter the electron density of the particle surface, affecting the surface plasmon absorption band.
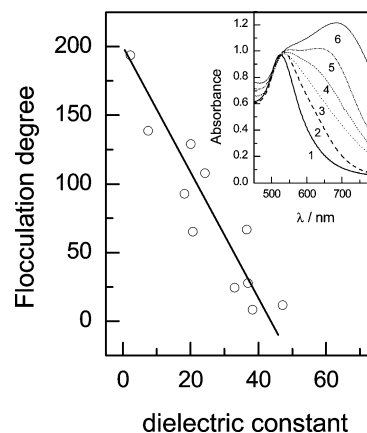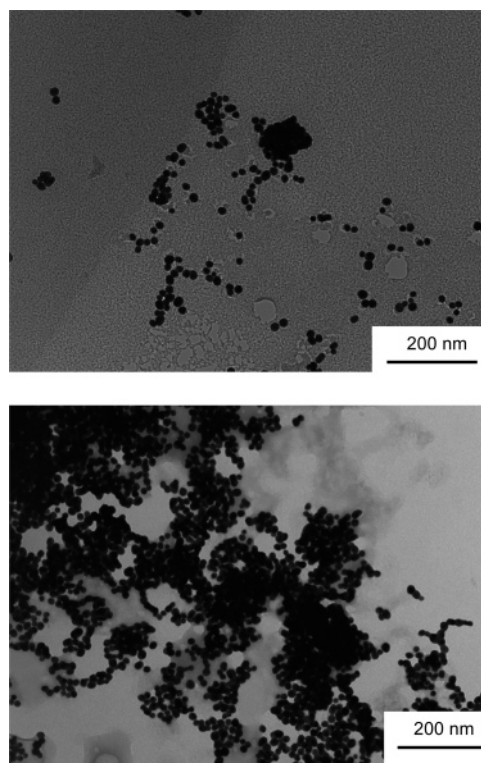

Figure 9. Representative TEM micrographs of 6MP−AuNPs suspended in acetonitrile (top) and ethanol (bottom).

The 6MP−AuNPs are soluble in water and other polar organic solvents. However, in most cases they flocculate as is manifested by the sudden color change and the shift of the absorption band to longer wavelengths. In the case in which the nanoparticles are soluble a red shift in the maximum absorption wavelength with the refractive index is observed that agrees with eq 4 (Figure 7). A g value of 0.619 can be calculated from the slope of this plot. However, if the core nanoparticle radius (∼6−7 nm) and the 6MP monolayer thickness (∼0.6−0.8 nm) are used in eq 5, the g value will oscillate between 0.2 and 0.3. Thus, this higher experimental g value should mean that the protection against the effect of the solvent refractive index of the AuNP by the 6MP shell is higher than that expected from a monolayer of similar thickness.

17846 *J. Phys. Chem. B, Vol. 110, No. 36, 2006*

Viudez et al.

On the other hand, it is interesting to note that the flocculation of the 6MP−AuNPs in organic solvent follows a clear trend in the sense that a higher flocculation degree is found when the dielectric constant of the solvent decreases, as is shown in Figure 8 (the dielectric constants for the solvents used to build this graph differ from those used in Figure 7 in that these values include orientation polarization effects due to the existence of a permanent dipole moment in such molecules[55,56]). The dispersibility of particles capped by a molecular layer in organic solvents depends on the interaction between the capping molecules and the solvent instead of the ionic double layer; that is, if the interaction between the capping molecules and the solvent is larger than the attractive forces between particles, the particles can stably disperse in the solvent.[57] The size of the aggregates formed by 6MP−AuNPs in different solvents increases with decreasing dielectric constant, in agreement with the spectra, where a longer displacement is found following this trend. Figure 9 shows the TEM images of preparations in acetonitrile ($\epsilon = 36.6$) and ethanol ($\epsilon = 24.3$), where it can be observed that the size of the aggregates increases following the same tendency. Moreover, the maximum of the absorption band shifts to the red as the aggregates become longer.[41]

Conclusions

In this study, 6MP molecules have been used to modify AuNP surfaces. The fast displacement by 6MP of the citrate anions that act as protector agents of the nanoparticles against flocculation in water solutions avoids its irreversible aggregation.

The formation of an ordered 6MP monolayer on the gold particle surface is demonstrated by FTIR spectroscopy. The binding of 6MP through the 6-SH group is proved by the disappearance of the S−H stretching vibration upon modification. Some spectral features point to the implication of the two rings of the molecule in the interaction with gold, the second attachment being through the N(7) position. Moreover, the C−H stretching modes of the different tautomers existent in free 6MP should be transformed to those corresponding to the thiol tautomer as is indicated by the disappearance of some bands and the important increase in intensity of those that remain upon modification.

The 6MP−AuNPs formed in an alkaline medium can be precipitated by centrifugation and then redissolved without any signal of aggregation. However, the stability is strongly dependent on the ionic strength and pH of the aqueous solution where they are dispersed as is typical of colloids that are stabilized by charged double-layer repulsion.[43,44] Thus, at pH lower than 7, the color of the solutions changes to blue, and this change is accompanied by a red-shifting and broadening of the SPR band, indicating that the distances between flocculating spheres is small compared to the radius of the spheres. This fact is also evidenced by TEM, where it can be observed that the particles tend to form aggregates of different sizes. It is interesting to note that the nanoparticle cores are not fused, showing a separation layer that amounts to two monolayers of 6MP. One important finding in this work is the fact that the 6MP−AuNPs that have flocculated in an acidic medium recover their dispersibility upon changing the solution pH to values above pH 7.

Finally, the effect of different organic media on the stability of 6MP−AuNP dispersions has also been studied. It has been found that they remain stable in some solvents where they behave according to the Mie theory if the organic monolayer is accounted for in the calculation, in a manner similar to that reported by Mulvaney et al.[10] However, the protection of the 6MP shell layer against the effect of the solvent refractive index is higher that that expected from a monolayer of similar thickness. On the other hand, other solvents induce flocculation, indicating that the interaction between the capping molecules and the solvent is lower than the attractive forces between particles. A correlation between the sizes of the aggregates and the magnitude of the solvent dielectric constants has been found.

References and Notes

(1) Schmid, G. *Chem. Rev.* **1992**, *92*, 1709.

(2) Daniel, M. C.; Astruc, D. *Chem. Rev.* **2004**, *104*, 293.

(3) Shipway, A. N.; Katz, E.; Willner, I. *ChemPhysChem* **2000**, *1*, 18.

(4) Handley, D. A. *Colloidal Gold. Principles, Methods and Applications*; Academic Press: New York, 1989.

(5) Turkevich, J.; Stevenson, P. C.; Hillier, J. *Discuss. Faraday Soc.* **1951**, 55.

(6) Ahmadi, T. S.; Wang, Z. L.; Henglein, A.; ElSayed, M. A. *Chem. Mater.* **1996**, *8*, 1161.

(7) Yee, C.; Scotti, M.; Ulman, A.; White, H.; Rafailovich, M.; Sokolov, J. *Langmuir* **1999**, *15*, 4314.

(8) Brust, M.; Walker, M.; Bethell, D.; Schiffrin, D. J.; Whyman, R. *J. Chem. Soc., Chem. Commun.* **1994**, 801.

(9) Brust, M.; Fink, J.; Bethell, D.; Schiffrin, D. J.; Kiely, C. *J. Chem. Soc., Chem. Commun.* **1995**, 1655.

(10) Templeton, A. C.; Pietron, J. J.; Murray, R. W.; Mulvaney, P. *J. Phys. Chem. B* **2000**, *104*, 564.

(11) Shon, Y.-S.; Mazzitelli, C.; Murray, R. W. *Langmuir* **2001**, *17*, 7735.

(12) Cliffel, D. E.; Zamborini, F. P.; Gross, S. M.; Murray, R. W. *Langmuir* **2000**, *16*, 9699.

(13) Aguila, A.; Murray, R. W. *Langmuir* **2000**, *16*, 5949.

(14) Kometani, N.; Tsubonishi, M.; Fujita, T.; Asami, K.; Yonezawa, Y. *Langmuir* **2001**, *17*, 578.

(15) Chen, S. H.; Kimura, K. *Langmuir* **1999**, *15*, 1075.

(16) Mulvaney, P. *Langmuir* **1996**, *12*, 788.

(17) Link, S.; El-Sayed, M. A. *J. Phys. Chem. B* **1999**, *103*, 8410.

(18) Frens, G. *Nature (London), Phys. Sci.* **1973**, *241*, 20.

(19) Weisbecker, C. S.; Merritt, M. V.; Whitesides, G. M. *Langmuir* **1996**, *12*, 3763.

(20) Fujiwara, H.; Yanagida, S.; Kamat, P. V. *J. Phys. Chem. B* **1999**, *103*, 2589.

(21) Kamat, P. V. *J. Phys. Chem. B* **2002**, *106*, 7729.

(22) Aslan, K.; Perez-Luna, V. H. *Langmuir* **2002**, *18*, 6059.

(23) Lin, S. Y.; Tsai, Y. T.; Chen, C. C.; Lin, C. M.; Chen, C. H. *J. Phys. Chem. B* **2004**, *108*, 2134.

(24) Madueno, R.; Sevilla, J. M.; Pineda, T.; Roman, A. J.; Blazquez, M. *J. Electroanal. Chem.* **2001**, *506*, 92.

(25) Madueno, R.; Pineda, T.; Sevilla, J. M.; Blazquez, M. *Langmuir* **2002**, *18*, 3903.

(26) Madueno, R.; Pineda, T.; Sevilla, J. M.; Blazquez, M. *J. Electroanal. Chem.* **2005**, *576*, 197.

(27) Terrill, R. H.; Postlethwaite, T. A.; Chen, C. H.; Poon, C. D.; Terzis, A.; Chen, A. D.; Hutchison, J. E.; Clark, M. R.; Wignall, G.; Londono, J. D.; Superfine, R.; Falvo, M.; Johnson, C. S.; Samulski, E. T.; Murray, R. W. *J. Am. Chem. Soc.* **1995**, *117*, 12537.

(28) Keating, C. D.; Musick, M. D.; Keefe, M. H.; Natan, M. J. *J. Chem. Educ.* **1999**, *76*, 949.

(29) Lapinski, L.; Nowak, M. J.; Kwiatkowski, J. S.; Leszczynski, J. *J. Phys. Chem. A* **1999**, *103*, 280.

(30) Szeghalmi, A. V.; Leopold, L.; Pinzaru, S.; Chis, V.; Silaghi-Dumitrescu, I.; Schmitt, M.; Popp, J.; Kiefer, W. *J. Mol. Struct.* **2005**, *735−736*, 103.

(31) Yang, H.; Liu, Y.; Liu, Z.; Yang, Y.; Jiang, J.; Zhang, Z.; Shen, G.; Yu, R. *J. Phys. Chem. B* **2005**, *109*, 2739.

(32) Chu, H.; Yang, H.; Huan, S.; Shen, G.; Yu, R. *J. Phys. Chem. B* **2006**, *110*, 5490.

(33) Johnson, S. R.; Evans, S. D.; Mahon, S. W.; Ulman, A. *Langmuir* **1997**, *13*, 51.

(34) Vivoni, A.; Chen, S. P.; Ejeh, D.; Hosten, C. M. *Langmuir* **2000**, *16*, 3310.

(35) Shipway, A. N.; Lahav, M.; Gabai, R.; Willner, I. *Langmuir* **2000**, *16*, 8789.

(36) Fox, J. J.; Wempen, I.; Hampton, A.; Doerr, I. L. *J. Am. Chem. Soc.* **1958**, *80*, 1669.

6-Mercaptopurine-Modified Gold Nanoparticles

J. Phys. Chem. B, Vol. 110, No. 36, 2006 **17847**

(37) Moore, D. E.; Sik, R. H.; Bilski, P.; Chignell, C. F.; Reszka, K. J. *Photochem. Photobiol.* **1994**, *60*, 574.

(38) Mie, G. *Ann. Phys.* **1908**, *25*, 377.

(39) Underwood, S.; Mulvaney, P. *Langmuir* **1994**, *10*, 3427.

(40) Wiesner, J.; Wokaun, A. *Chem. Phys. Lett.* **1989**, *157*, 569.

(41) Quinten, M.; Kreibig, U. *Surf. Sci.* **1986**, *172*, 557.

(42) Mayya, K. S.; Patil, V.; Sastry, M. *Langmuir* **1997**, *13*, 3944.

(43) Reerink, H.; Overbeek, J. T. G. *Discuss. Faraday Soc.* **1954**, 74.

(44) Ottewill, R. H.; Walker, T. *Kolloid Z. Z. Polym.* **1967**, *227*, 108.

(45) Marinovic, V.; Despic, A. R. *J. Electroanal. Chem.* **1997**, *431*, 127.

(46) Albert, A.; Brown, D. J. *J. Chem. Soc.* **1954**, 2060.

(47) Zhong, C.-J.; Woods, N. T.; Dawson, G. B.; Porter, M. D. *Electrochem. Commun.* **1999**, *1*, 17.

(48) Cohen-Atiya, M.; Mandler, D. *J. Electroanal. Chem.* **2003**, *550−551*, 267.

(49) Kakiuchi, T.; Iida, M.; Imabayashi, S. i.; Niki, K. *Langmuir* **2000**, *16*, 5397.

(50) McConnell, T. L.; Wheaton, C. A.; Hunter, K. C.; Wetmore, S. D. *J. Phys. Chem. A* **2005**, *109*, 6351.

(51) Sastry, M.; Mayya, K. S.; Bandyopadhyay, K. *Colloids Surf., A* **1997**, *127*, 221.

(52) Giersig, M.; Mulvaney, P. *Langmuir* **1993**, *9*, 3408.

(53) Ghosh, S. K.; Nath, S.; Kundu, S.; Esumi, K.; Pal, T. *J. Phys. Chem. B* **2004**, *108*, 13963.

(54) Thomas, K. G.; Zajicek, J.; Kamat, P. V. *Langmuir* **2002**, *18*, 3722.

(55) Laurence, C.; Nicolet, P.; Dalati, M. T.; Abboud, J. L. M.; Notario, R. *J. Phys. Chem.* **1994**, *98*, 5807.

(56) Abboud, J. L. M.; Notario, R. *Pure Appl. Chem.* **1999**, *71*, 645.

(57) Huang, S. H.; Minami, K.; Sakaue, H.; Shingubara, S.; Takahagi, T. *J. Appl. Phys.* **2002**, *92*, 7486.