Synthesis of Amphiphilic Hyperbranched Polyglycerol Polymers and Their Application as Template for Size Control of Gold Nanoparticles

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ABSTRACT: Amphiphilic thioether-containing core-shell polymers were synthesized by two-step reaction of hyperbranched polyglycerol (PG): first the hydroxyls of PG were O-alkylated with 1-bromo-3-chloropropane by improved Williamson reaction, and 31.6% of the hydroxyls were transformed to allyl groups and 22.4% of hydroxyls to 3-chloropropyl; then the residual 3-chloropropyl groups were efficiently S-alkylated with 1-dodecanethiol. Thus the amphiphilic polymers composed of hydrophobic thioether-containing shell and hydrophilic PG core were formed and could be used as template for the synthesis of zero-valent gold nanoparticles by the coordination interaction between gold species and thioether. The resulting colloids were stable and the size of the encapsulated gold nanoparticles could be adjusted by changing the molecular weight/size of the PG core of the amphiphilic derivatives. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 101: 509–514, 2006

Key words: core-shell polymer; hyperbranched; templates; gold nanoparticle; size control

INTRODUCTION

Nanoscale core-shell organized polymers have evoked much interest because they could be used to encapsulate guest molecules,[1] stabilize inorganic nanoparticles,[2,3] and improve the solubility of some materials.[4] It also showed a great potential as catalyst support[2,3] and biomedical delivering "nanobox."[5] Wooley[6,7] and Armes[8–10] have utilized a variety of amphiphilic block copolymers to synthesize numerous shell crosslinked knedel-like core-shell polymer nanoparticles by combination of physical self-assembly with chemical immobilization.

Recently, hyperbranched polymers[11] were successfully employed to encapsulate guest molecules[12,13] and ionic catalytic metals.[14] In contrast to dendrimers,[15] which were generally tediously prepared and were with limited growth, many hyperbranched polymers could be synthesized in one step from AB_n-type ($n \geq 2$) monomers and could be produced in large quantities and thus cost-effective.[16]

Hyperbranched polyglycerol (PG)[11] was one important hyperbranched polymer, which can be synthesized in one-pot with commercially available glycidol. Its hydroxyl groups distributed throughout the global structure and constituted a platform of a variety of chemical modifications. PG based amphiphilic polymers showed interesting property as encapsulating various polar, water-soluble dye molecules,[12,13] or ionic metal catalyst[14] and transferring them to apolar media. Such properties also constituted the potential biomedical application.[5]

On the other hand, zero-valent transition metal nanoparticles have widely used in bioassay,[17] catalytic chemistry[18] and so on; therefore an idea was suggested by us—could we use these hyperbranched PG to control the size of transition metal nanoparticles? Brust[19] synthesized uniform gold nanoparticles (AuNPs) using aliphatic thiol as mediator for the first time; he indicated that the monolayer thiol protected gold colloids showed the several advantages of easy separation, good solubility in various solvents, air stability, and isolation as a solid. Reinhoudt and colleagues[20–22] further developed this technique by using multi-thioether ligands, but the synthesis involving multi-thioether was generally tedious and the yield was low. Here we describe an efficient synthesis of a novel thioether-containing amphiphilic derivative of hyperbranched PG, its application in synthesis of AuNPs, its effect on size control, and stability of the resulting particles.

EXPERIMENTAL

Materials

Tetraoctylammonium bromide, ethanol, $Br(CH_2)_3Cl$, $Br(CH_2)_4Cl$, potassium hydroxide, potassium carbon-

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ate, $HAuCl_4$, dimethyl sulfoxide (DMSO), poly(ethylene glycol methyl ether) (molecular weight 550), glycidol, poly(propylene oxides) 1000, 2000, and 4000, sodium borohydride, chloroform, toluene, and 1-dodecanelthiol were purchased from Aldrich or Acros and used directly; 1,1,1-Tris(hydroxymethyl) propane (TMP), potassium methylate solution (3.7*M* in methanol) were purchase from Fluka; Poly(propylene oxides) with molecular weight 8000 and 12,000 were the products of ARCO Chemical Co.; Benzil was purchased from Merck. Benzoylated dialysis tubing (D-7884, MWCO 1200) was obtained from Sigma

Preparation of PG[11] (1a,1b)

Polymerization was carried out in a reactor equipped with a mechanical stirrer and dosing pump under argon atmosphere. Typically, 1,1,1-Tris(hydroxymethyl)propane (2.78 g) was 10% deprotonated with 0.7 mL of potassium methylate solution (3.7*M* in methanol) by distilling off excess methanol from the melt. A 50 g aliquot of glycidol was slowly added at 95°C over 12 h. The product was dissolved in methanol and neutralized by filtration over cation-exchange resin. The polymer was twice precipitated from methanol solution into acetone and subsequently dried for 15 h at 80°C in vacuo. PG (42.7 g) with molecular weight 2000 (**1a**) was obtained as a transparent, highly viscous liquid in yield of 80% [M_n = 2000 (VPO) and M_w/M_n = 1.4 (GPC), average 27 hydroxyls each molecule,[11] 13.5 mmol OH/g (PG)]. A polymer with molecular weight of 8000 (**1b**) was synthesized using the same procedure [M_n = 8000 (VPO) and M_w/M_n = 1.38 (GPC)]. ^{1}H NMR (CD_3OD, δ/ppm): 0.82 (t, CH_3 of TMP), 1.25 (tetra, CH_2 of TMP), 3.0–4.1 (m, CH and CH_2 of monomer unit).

Synthesis of *O*-alkylated PG (2a,2b)

Typically, to a solution of 5 g (67.5 mmol OH) PG **1a** or **1b** in 9 mL DMSO potassium hydroxide (7.56 g, 2 equiv. of hydroxyl), 1-bromo-3-chloropropane (30 mL, 4.5 equiv of hydroxyl) and 3 mL polyethylene oxide (molecular weight: 550), as a phase transfer catalyst, were added.[23–25] The system was allowed to stir for 18 h at 40°C, the interface between upper layer of DMSO-PG phase and the lower layer of halogen phases gradually fade away with the progress of the reaction. After filtration of the inorganic salt and removal of DMSO and excessive 1-bromo-3-chloropropane under reduced pressure at 120°C, the residual was washed with distilled water for three times and dried in chloroform by magnesium sulfate, the final separated colorless oil weighted 6.5 g after dryness in vacuo. ^{1}H NMR($CDCl_3$), δ(ppm): 1.25(t, CH_2 of TMP), 1.90 (—$OCH_2CH_2CH_2Cl$), 3.41 (—CH_2Cl), 3.53(—OCH_2—), 3.30–3.90 (m, CH_2 and CH of polyglycerol), 3.88, 4.01 ($OCH_2CH{=}CH_2$), 5.05–5.18 ($CH{=}CH_2$), 5.97 ($CH{=}CH_2$). ^{13}C NMR ($CDCl_3$), δ(ppm): signals independent of polyglycerol: 32.94, 32.46 (—$OCH_2CH_2CH_2Cl$), 40.76, 41.84 (—$OCH_2CH_2CH_2Cl$), 70.43, 71.08 (—$OCH_2CH_2CH_2Cl$), 78.71, 78.64 ($OCH_2CH{=}CH_2$), 117.04 ($CH{=}CH_2$), 134.64 ($CH{=}CH_2$), and 61.88, 63.57, 66.55, 67.71, 70.43, 71.18, 72.21 ppm for PG.[11]

Synthesis of S-alkylated PG (3a,3b)

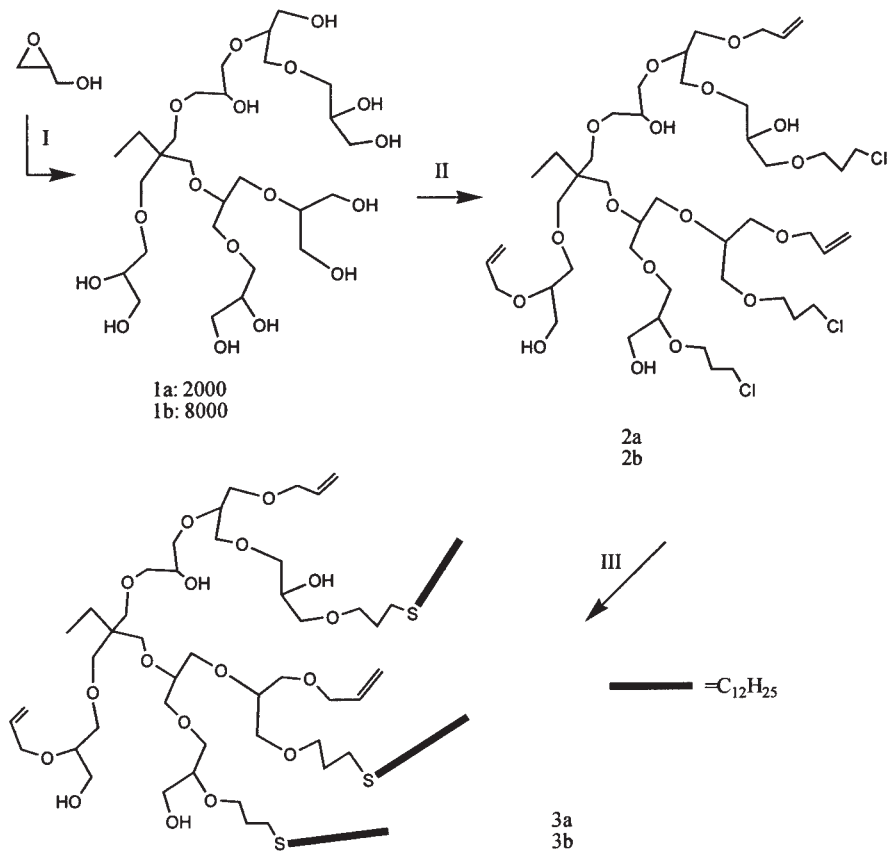
S-alkylation of PG **2a** or **2b** was typically carried out as follows: 20 mL acetone containing 1.46 g of PG **2a** was charged in a three neck flask, 0.4 g (3.96 mmol) potassium carbonate was added with magnetic stirring under argon, followed by addition of 0.76 mL (3.2 mmol) of 1-dodecanethiol dropwise under refluxing within 1.5 h, later followed by refluxing for 12 h. After removal of the inorganic salt and acetone, the polymer was purified by dialysis against chloroform, 1.95 g (98%) viscous oil was obtained. ^{1}H NMR($CDCl_3$), δ(ppm): 0.86 (t, CH_3), 1.24–1.45 (—$SCH_2CH_2(CH_2)_9CH_3$), 1.54 (—SCH_2CH_2—), 1.81 (—$OCH_2CH_2CH_2S$—), 2.47 (—SCH_2CH_2—), 2.59 (—$OCH_2CH_2CH_2S$—), 3.62 (—OCH_2), 3.30–3.90 (m, polyglycerol), 4.11, 3.99 ($OCH_2CH{=}CH_2$), 5.10–5.24 ($CH{=}CH_2$), 5.82 ($CH{=}CH_2$).

Preparation of gold nanoparticles

The syntheses were carried out by following method developed by Brust et al.[19]: the molar ratio of reactants was Au : S : N^+R_4 : $NaBH_4$ = 1 : 3 : 2 : 12. Typically, 65 mg (0.19 mmol) $HAuCl_4$ in water was mixed with 380 mg of PG **3a** and 218 mg tetraoctylammonium bromide in 25 mL toluene, the mixture was stirred vigorously for a while, then the organic layer was separated, to which 86 mg (2.27 mmol) fresh $NaBH_4$ in 15 mL water was added dropwise under stirring and the mixture was kept on stirring for 0.5 h, then the mixture was allowed to stand by for 2 days. The precipitate was discarded and the clear solution was washed with distilled water for 3 times, the organic layer was subjected to rotary evaporation to remove the toluene. The residual brownish solid was dissolved in ethanol and collected by centrifugation to remove the residual $(n\text{-octyl})_4NBr$, finally, the solid was dried under vacuum at room temperature before UV–vis detection or TEM measurement.

Measurements

^{1}H and ^{13}C NMR were recorded on Bruker AMX 300. UV–vis spectra were recorded on a PerkinElmer Lambda 2. Gel permeation chromatography (GPC) were performed by a Knauer microgel set C11 using DMF as an eluent at 45°C with a concentration of 5



I: 1,1,1-tris(hydroxymethyl)propane (TMP)/$NaOCH_3$, 95°C; II: 1-bromo-3-chloropropane/DMSO, PEO, KOH, 40°C; III: K_2CO_3/acetone, dodecanethiol, reflux.

Scheme 1 Schematic synthesis of polyglycerol, its modification by O-alkylation and S-alyklation (in Scheme 1, **1a**, **1b** represent polyglycerol with molecular weight of 2000 and 8000, respectively; the scheme showed a polymer with one initiator (core molecule TMP) while only 7 monomer units were shown for simplicity).

mg/mL, and a evaporative mass detector EMD 960 (Polymer Labaratories) operating at 110°C; poly(propylene oxides) 1000, 2000, 4000 (Aldrich), 8000, and 12,000 (ARCO Chemical Co.) were used for calibration. Vapor pressure osmometry (VPO) was carried out using a Knauer vapor pressure osmometer in methanol at 45°C in a concentration range of 5–10 mg/mL, and benzil was used for calibration. The size of AuNPs was analyzed using a LEO 912 Omega transmission electronic microscopy (TEM) operating at an acceleration voltage of 120 kV on a carbon-coated copper grid.

RESULTS AND DISCUSSION

O-alkylation of PG by improved Williamson reaction

The synthesis of the target polymers was shown in Scheme 1. The degree of branching (DB) of PG was derived by a slow monomer addition technique[11]; the value is in the range of 0.52–0.59. By comparing hyperbranched PG with its linear PG counterpart, we found that (1) the content of hydroxyls is 13.5 mmol/g for both polymer[26]; (2) one branching site is equivalent to changing one pendant hydroxyl to one terminal hydroxyl.[27] Thus, it could be derived from the DB value (0.52–0.59) that the amount of terminal hydroxyls of one hyperbrached PG roughly made up 52–59% of its total number of hydroxyls.

In the process of introducing halogen group onto PG, it was found that if the hydroxyls of PG were O-alkylated directly with 1-bromo-3-Chloropropane by conventional Williamson reaction (NaH, alkyl halide, dimethylformamide), the reaction is incomplete and poorly controlled, and an intermediate of PG with so poor solubility was formed. Thus the improved Williamson asymmetric etherification was suggested (Scheme 1) by us, in which the O-alkylation of hydroxyls of PG was carried out in the presence of phase transfer catalyst and NaOH; the reaction is efficient, mild and simple.[23–25]

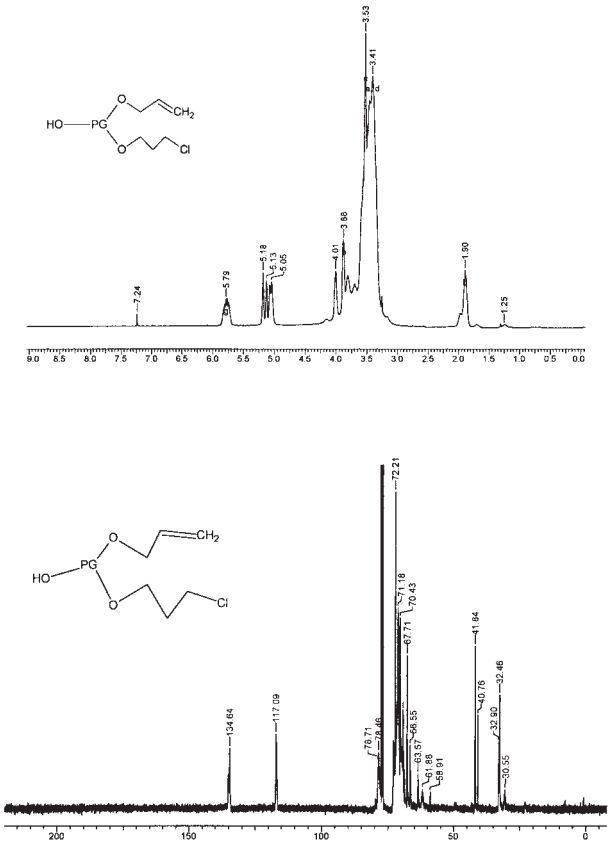


Figure 1 ^{1}H NMR (top) and ^{13}C NMR (bottom) of **2a** in $CDCl_3$ (PG: polyglycerol).

Figure 1 showed ^{1}H NMR and ^{13}C NMR spectra of the *O*-alkytaled PG **2a** prepared by improved Williamson reaction, and the attribution of the peaks was listed in the experimental part. It was found that there appeared some peaks for double bond except the peaks for chloropropyl and PG. In our improved Williamson conditions, there were three phases of polar DMSO, apolar 1-bromo-3-chloropropane and solid NaOH. The polar DMSO medium favored substitution of halide while aploar medium favors elimination of halide. Thus in polar DMSO phase, elimination of hydrogen bromide from1-bromo-3-chloropropane was unfavorable; however, a HBr molecule could be easily eliminated from 1-bromo-3-chloropropane under base conditions in aploar 1-bromo-3-chloropropane phase, and allyl chloride was thus formed. According to the simple calculation of the integration area in Figure 1, it could be derived that 22.4% of hydroxyls were transformed into *O*-3-chloropropyl based on the ratio of the signal at 1.90 ppm (2H, $CH_2CH_2CH_2Cl$) and the signals at 3.0–4.3 ppm (overlap of polyglycerol and $CH_2CH_2CH_2Cl$) for **2a** and **2b**. Similarly, based on the area ratio of signal at 5.97 ppm (1H, $—CH═CH_2$) to signal at 1.90 ppm (2H, $CH_2CH_2CH_2Cl$), it could also be derived that 31.6% of hydroxyls were transformed into *O*-allyl groups for **2a** and **2b**.

S-alkylation of *O*-3-Chloropropyl on PG

The modification of polymers involving multi-thiol or multi-thioether was generally tedious and yield was low because of side reaction, especially the oxidative crosslinking between thiols. In our reaction, the synthesis involving multi-thioether was highly efficient because reaction involving multi-thiol intermediate was avoided. The *O*-alkylated PG was directly reacted with 1-dodecanthiol to form amphiphilic polymers with multi-thioether. Figure 2 showed the ^{1}H NMR of *S*-alkylated PG, and the assignation of peaks was also listed in the experimental part. The thioether content for both **3a** and **3b** could be calculated from the ^{1}H NMR spectrum (Fig. 2) by comparing the area ratio at 0.86 ppm (3H, CH_3) and 5.82 ppm (1H, $CH═CH_2$), and the molar ratio of these two groups was about 1:1.4. This value is the same as the ratio of 3-chloropropyl and allyl (22.4% : 31.6%), and it means the chlorine end group was 100% *S*-alkylated. Based on 1 g polyglycerol, after the aforementioned modification, 4.3 mmol (31.6% of the 13.5 mmol hydroxyls) were transformed to allyl groups, and 3.02 mmol (22.4% of the 13.5 mmol hydroxyls) to thioether. Therefore, after the modification, the polymer weight would increase to 1.91 g, and the content of thioether is 1.58 mmol per gram of polymer.

Effect of amphiphilic PG on synthesis of gold nanoparticles

PG **3a**, **3b** were the amphiphilic polymers with core-shell structure, in which the substituted dodecyl groups constituted the hydrophobic shell and residual hydroxyls of PG constituted hydrophilic part of the core. The synthesis of AuNPs was carried out by close following of the method of Brust[19] and Reinhoudt.[20–22] Upon reduction of gold ions, the system became brown, indicating the formation of zero-valent gold nanoparticles, and the change of color was detected by UV–vis spectra shown in Figure 3. It could

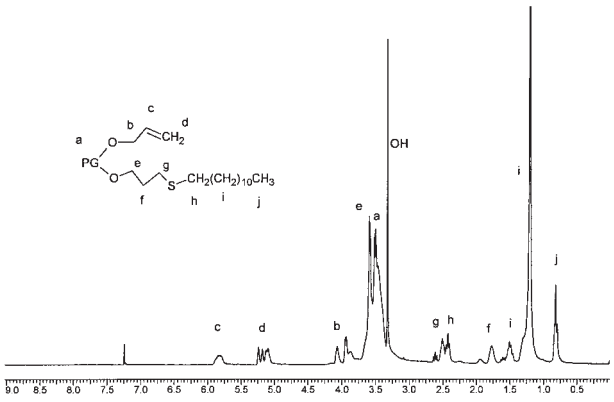


Figure 2 ^{1}H NMR of **3a** in $CDCl_3$ (PG: polyglycerol).

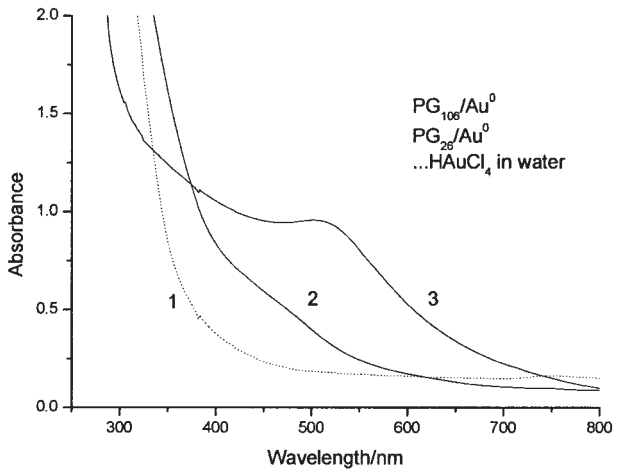


Figure 3 UV–vis spectra of $HAuCl_4$ (1) in water and gold nanoparticle mediated by **3a** (2) and **3b** (3) in chloroform.

be found that the absorbance of AuNPs mediated by **3a** and **3b** were quite different; the absorbance at 515 nm was very weak for the former, while there was a strong surface plasma resonance band at 515 nm for the latter. The surface plasma resonance band was a feature of AuNPs larger than 4 nm[28]; this means that most AuNPs mediated by **3a** were smaller than 4 nm, while most of those mediated by **3b** were larger than 4 nm. Figure 4 showed the transmission electronic microscopy of the particle sizes; the average size of gold nanoparticles mediated by **3a** was 3.0 ± 1.6 nm, while that by **3b** was 5.1 ± 2.4 nm. Moreover, in our system, the AuNPs could be obtained as a solid and dispersed in the organic solvents such as chloroform or THF to form a clear colloid, and all the colloids could keep clear for at least six months. As everyone knows that in the preparation of AuNPs, surfactants[29] have been widely used, but the stability of AuNPs was problematic in rigorous chemical environment because of dynamic ligand exchange. Our results showed that the PG with only 22.4% dodecyl thioether could sufficiently stabilize the in situ produced AuNPs.

The size control of AuNPs might be related with the reverse micelle-like structure of the polymer template. It has been shown that analogues of such unimolecular micelle could encapsulate guest molecules, and the capacity is directly dependent on the size/molecular weight of the core PG molecule. The larger PG showed higher capacity.[12] In our case, the distribution and amount of thioether groups of one template polymer are highly dependent on the size/molecular weight of the core PG molecule, and a spheric periphery around the PG molecule was formed by thiother groups. Owing to the affinity between thioether and gold species, the thioether periphery might constitute the compartment for the gold nanoparticles, while the alkyl shell constituted the protecting layer. Thus the size of AuNPs was strongly affected by the size/molecular weight of the amphiphilic template. The higher the molecular weight of PG, the more the amount of thiother; therefore the stronger the control of template polymers for the AuNPs.

CONCLUSIONS

O-alkylation of the hydroxyls of hyperbranched PG with 1-bromo-3-chloropropane was carried out in the improved Williamson reaction, 22.4% of the hydroxyls of PG was substituted by 3-chloropropyl and 31.6% by allyl. After further S-alkylation of the 3-chloropropyl, an amphiphilic PG with core-shell structure was formed. It could be used to stabilize gold nanoparticles in situ produced, and the gold particle sizes

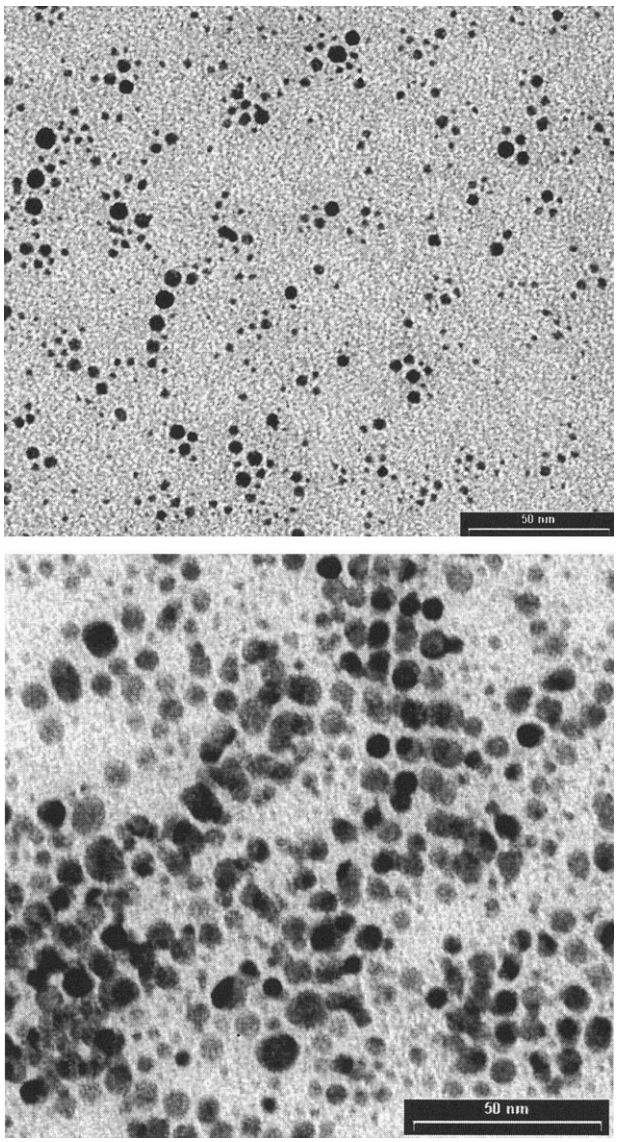


Figure 4 TEM micrograph of gold nanoparticles mediated by **3a** (top) and **3b** (bottom). Scale bar: 50 nm.

could be controlled by variation of molecular weight of PG.

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