4-(*N*,*N*-Dimethylamino)pyridine-Protected Au Nanoparticles: Versatile Precursors for Water- and Organic-Soluble Gold Nanoparticles

Simona Rucareanu, Valérie J. Gandubert, and R. Bruce Lennox*

Department of Chemistry and Centre for Self-Assembled Chemical Structures (CSACS), McGill University, 801 Sherbrooke Street West, Montréal, Québec, H3A 2K6, Canada

Received April 4, 2006. Revised Manuscript Received July 7, 2006

Ligand-exchange reactions of 4-(*N*,*N*-dimethylamino)pyridine-capped gold nanoparticles (DMAP−Au NP) with functionalized thiols (RSH) were investigated. A simple, convenient, and facile synthesis method has been developed. An important feature of this method is its requirement of only very modest quantities of excess thiol ligand. DMAP−Au NP prove to be versatile precursors for both water- and organic-soluble gold NP. DMAP is readily displaced by various functionalized thiols ranging from mercaptocarboxylic acids to ferrocene-terminated thiols. UV−vis spectroscopy and transmission electron microscopy (TEM) confirm that the mean diameter and the size dispersity of the initial DMAP−Au NP were retained upon ligand exchange. The RS−Au NP thus prepared were efficiently purified by gel permeation chromatography (GPC) with neither residual DMAP nor RSH detected in the final product.

Introduction

The use of monolayer-protected gold nanoparticles (NP) in applications related to catalysis,[1−3] sensors,[4,5] molecular markers, biolabeling,[6,7] and drug delivery[8] creates the need for new preparative methods which can enable control over particle size, dispersity, solubility, and functionality. While substantial progress from a synthetic standpoint has been made since the Brust−Schiffrin procedure[9] was reported in 1994, there still is a real need for methods which lead to functionalized NP. Although the two-phase Brust−Schiffrin method[9] is valuable in preparation of small NP (1−3 nm) soluble in organic solvents, it has the shortcoming of having persistent residual tetraoctylammonium bromide (TOAB). The TOAB is often retained even after repetitive precipitation and washing with ethanol or acetone.[10,11] Alternative single-phase syntheses avoid the use of a transfer agent.[12−15] This approach is particularly attractive because it can provide access to water-soluble NP.[12,13] The direct synthesis procedures involving gold salts and suitable stabilizing ligands, in both one- or two-phase approaches, are widely used to prepare monolayer-protected gold NP. Nonetheless, these methodologies are often tedious in the workup stage. They are also restricted to capping ligands compatible with the reductive agent (sodium borohydride or Superhydride). Finally, these methods offer limited control over size and dispersity.

The alkylthiol-for-alkylthiol place-exchange reactions described by Murray and co-workers[16,17] offer an approach to functionalized gold NP using presynthesized NP. Although easy to perform, the procedure requires considerable excess of incoming ligand and invariably leads to mixed monolayers.[16,18] Complete displacement of the initial ligand is difficult to achieve even in the presence of a large excess of incoming thiol when an alkylthiol is used as initial capping ligand. Considerable work has recently been performed in order to elucidate the ligand-exchange mechanism.[18−22] Although still not fully understood, the place-exchange process represents an opportunity to use starting materials such as citrate-[23−28] and phosphine-stabilized Au NP.[29−33] Both citrate and

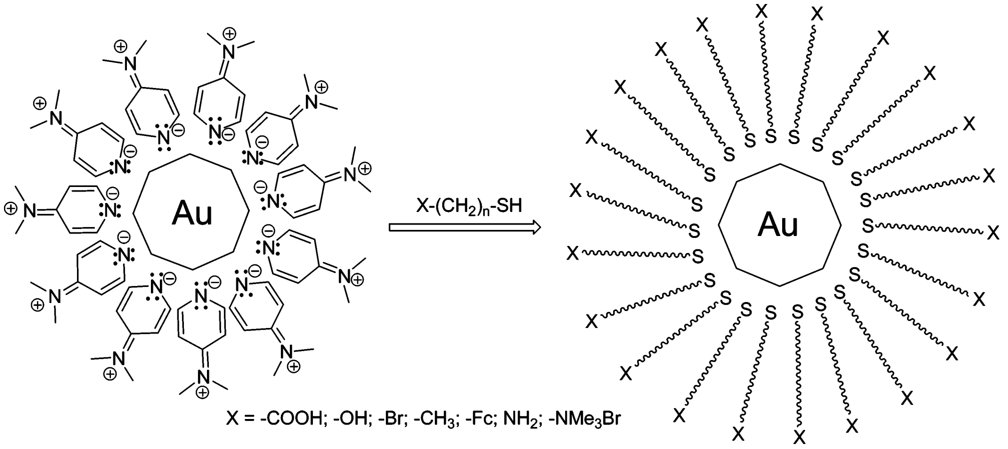
---

* To whom correspondence should be addressed. E-mail: Bruce.Lennox@mcgill.ca.

(1) Mohr, C.; Hofmeister, H.; Radnik, J.; Claus, P. *J. Am. Chem. Soc.* **2003**, *125*, 1905−1911.
(2) Zhong, C.-J.; Maye, M. M. *Adv. Mater.* **2001**, *13*, 1507−1511.
(3) Haruta, M. *Catal. Today* **1997**, *36*, 153−166.
(4) Zayats, M.; Kharitonov, A. B.; Pogorelova, S. P.; Lioubashevski, O.; Katz, E.; Willner, I. *J. Am. Chem. Soc.* **2003**, *125*, 16006−16014.
(5) Willner, I.; Willner, B. *Pure Appl. Chem.* **2002**, *74*, 1773−1783.
(6) Jahn, W. *J. Struct. Biol.* **1999**, *127*, 106−112.
(7) Hainfeld, J. F. *Science* **1987**, *236*, 450−453.
(8) Hone, D. C.; Walker, P. I.; Evans-Gowing, R.; FitzGerald, S.; Beeby, A.; Chambrier, I.; Cook, M. J.; Russell, D. A. *Langmuir* **2002**, *18*, 2985−2987.
(9) Brust, M.; Walker, M.; Bethell, D.; Schiffrin, D. J.; Whyman, R. *J. Chem. Soc., Chem. Commun.* **1994**, 801−802.
(10) Rowe, M. P.; Plass, K. E.; Kim, K.; Kurdak, C.; Zellers, E. T.; Matzger, A. J. *Chem. Mater.* **2004**, *16*, 3513−3517.
(11) Waters, C. A.; Mills, A. J.; Johnson, K. A.; Schiffrin, D. J. *Chem. Commun.* **2003**, 540−541.
(12) Templeton, A. C.; Chen, S.; Gross, S. M.; Murray, R. W. *Langmuir* **1999**, *15*, 66−76.
(13) Chen, S.; Kimura, K. *Langmuir* **1999**, *15*, 1075−1082.
(14) Yee, C. K.; Jordan, R.; Ulman, A.; White, H.; King, A.; Rafailovich, M.; Sokolov, J. *Langmuir* **1999**, *15*, 3486−3491.
(15) Brust, M.; Fink, J.; Bethell, D.; Schiffrin, D. J.; Kiely, C. *J. Chem. Soc., Chem. Commun.* **1995**, 1655−1656.
(16) Hostetler, M. J.; Green, S. J.; Stokes, J. J.; Murray, R. W. *J. Am. Chem. Soc.* **1996**, *118*, 4212−4213.
(17) Templeton, A. C.; Wuelfing, W. P.; Murray, R. W. *Acc. Chem. Res.* **2000**, *33*, 27−36.
(18) Ingram, R. S.; Hostetler, M. J.; Murray, R. W. *J. Am. Chem. Soc.* **1997**, *119*, 9175−9178.
(19) Hostetler, M. J.; Templeton, A. C.; Murray, R. W. *Langmuir* **1999**, *15*, 3782−3789.
(20) Song, Y.; Murray, R. W. *J. Am. Chem. Soc.* **2002**, *124*, 7096−7102.
(21) Montalti, M.; Prodi, L.; Zaccheroni, N.; Baxer, R.; Teobaldi, G.; Zerbetto, F. *Langmuir* **2003**, *19*, 5172−5174.
(22) Kassam, A.; Bremner, G.; Clark, B.; Ulibarri, G.; Lennox, R. B. *J. Am. Chem. Soc.* **2006**, *128*, 3476−3477.

10.1021/cm060793+ CCC: $33.50

Scheme 1. DMAP−Au NP as Starting Material for Preparation of Water- and Organic-Soluble RS−Au NP



triphenylphosphine are labile ligands and are displaced by thiols under mild reaction conditions with no residual contamination from citrate or triphenylphosphine reported.[27,28,31,33] Triphenylphosphine−Au NP are thus important precursors for small NP (1−2 nm), and citrate-stabilized NP are valuable precursors for large NP (15−40 nm).

We have focused on DMAP−Au NP as a precursor for functionalized NP whose diameter is in the range of 4−6 nm. DMAP−Au NP have been shown to be useful for encapsulation by polyelectrolyte multilayers,[34−40] adsorption onto SAM,[41] or as templates to grow compact $CaCO_3$ particles.[42] Although the displacement of DMAP by another capping agent (triphenylphosphine-3,3′,3″-trisulfonic acid trisodium salt) has been mentioned,[43] no systematic evaluation has been reported to date. The present study investigates place-exchange reactions of DMAP on gold NP and concludes that DMAP−Au NP are indeed versatile precursors for RS−Au NP (Scheme 1 and Chart 1).

Experimental Section

Chemicals. Hydrogen tetrachloroaurate trihydrate ($HAuCl_4 \cdot 3H_2O$, 99.9999%) was purchased from Strem Chemicals. Tetraoctylammonium bromide (TOAB, 98%), sodium borohydride ($NaBH_4$, 99%), 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 99%), *n*-decanethiol ($C_{10}SH$, 97%), 11-mercaptoundecanol ($HOC_{11}SH$, 97%), 3-mercaptopropionic acid ($HOOCC_2SH$, 99%), 11-mercaptoundecanoic acid ($HOOCC_{10}SH$, 95%), 16-mercaptohexadecanoic acid ($HOOCC_{15}SH$, 90%), 2-aminoethanethiol hydrochloride ($H_2NC_2SH \cdot HCl$, 98%), 2-(*N*,*N*-dimethylamino)ethanethiol hydrochloride ($Me_2NC_2SH \cdot HCl$, 95%), and 5-[1,2]dithiolan-3-yl-pentanoic acid (thioctic acid) were received from Aldrich and used without further purification. 11-Bromoundecanethiol ($BrC_{11}SH$),[44] 11-aminoundecanethiol ($H_2NC_{11}SH$), and 14-mercaptotetradecanol ($HOC_{14}SH$) were available from previous studies. 12-Ferrocenyl-1-dodecanethiol ($FcC_{12}SH$) was prepared according to a described procedure.[45,46] TOAB−Au and DMAP−Au were synthesized using Gittins and Caruso's procedure[47] as described elsewhere.[48] Sephadex LH-20 (Amersham BioSciences) and Sephadex G-25−150 (Sigma-Aldrich) were swollen in suitable solvents and loaded into a glass column. Aluminum-backed silica thin-layer chromatography plates (250 μm thick) were purchased from Silicycle (Québec, Canada). Toluene (ACS grade), dichloromethane (ACS grade), hexane (ACS grade), and ethanol (95% and absolute) came from Fischer Scientific. Pure water of high resistivity (>18 MΩ) was obtained by using a Milli-Q water system (Millipore Corporation).

Instrumentation. UV−vis spectra were recorded at room temperature with a Cary 5000 UV−vis−NIR spectrophotometer (Varian Instruments) using 1 cm quartz cuvettes. ^{1}H NMR spectra were obtained on a Varian 400 MHz instrument using D_2O, CD_3OD, CD_2Cl_2, or $CDCl_3$ as solvents. Spectra are referenced to the residual protons in the deuterated solvent. Transmission electron microscopy (TEM) experiments were performed on a Philips

---

(23) Turkevich, J.; Stevenson, P. C.; Hillier, J. *Discuss. Faraday Soc.* **1951**, *11*, 55−75.

(24) Niemeyer, C. M.; Ceyhan, B.; Gao, S.; Chi, L.; Peschel, S.; Simon, U. *Colloid Polym. Sci.* **2001**, *279*, 68−72.

(25) Niemeyer, C. M.; Ceyhan, B.; Hazarika, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 5766−5770.

(26) Zhu, T.; Vasilev, K.; Kreiter, M.; Mittler, S.; Knoll, W. *Langmuir* **2003**, *19*, 9518−9525.

(27) Levy, R.; Thanh, N. T. K.; Doty, R. C.; Hussain, I.; Nichols, R. J.; Schiffrin, D. J.; Brust, M.; Fernig, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 10076−10084.

(28) Lin, S.-Y.; Tsai, Y.-T.; Chen, C.-C.; Lin, C.-M.; Chen, C.-h. *J. Phys. Chem. B* **2004**, *108*, 2134−2139.

(29) Brown, L. O.; Hutchison, J. E. *J. Am. Chem. Soc.* **1997**, *119*, 12384−12385.

(30) Brown, L. O.; Hutchison, J. E. *J. Am. Chem. Soc.* **1999**, *121*, 882−883.

(31) Woehrle, G. H.; Warner, M. G.; Hutchison, J. E. *J. Phys. Chem. B* **2002**, *106*, 9979−9981.

(32) Petroski, J.; Chou, M. H.; Creutz, C. *Inorg. Chem.* **2004**, *43*, 1597−1599.

(33) Woehrle, G.; Brown, L. O.; Hutchison, J. E. *J. Am. Chem. Soc.* **2005**, *127*, 2172−2183.

(34) Gittins, D. I.; Susha, A. S.; Schoeler, B.; Caruso, F. *Adv. Mater.* **2002**, *14*, 508−512.

(35) Yu, A.; Liang, Z.; Cho, J.; Caruso, F. *Nano Lett.* **2003**, *3*, 1203−1207.

(36) Liang, Z.; Susha, A.; Caruso, F. *Chem. Mater.* **2003**, *15*, 3176−3183.

(37) Dong, W.-F.; Sukhorukov, G. B.; Mohwald, H. *Phys. Chem. Chem. Phys.* **2003**, *5*, 3003−3012.

(38) Shchukin, D. G.; Caruso, R. A. *Chem. Commun.* **2003**, 1478−1479.

(39) Kim, B.; Sigmund, W. M. *Langmuir* **2004**, *20*, 8239−8242.

(40) Radt, B.; Smith, T. A.; Caruso, F. *Adv. Mater.* **2004**, *16*, 2184−2189.

(41) Jiang, P.; Morales, G. M.; You, W.; Yu, L. *Angew. Chem., Int. Ed.* **2004**, *43*, 4471−4475.

(42) Schwahn, D.; Balz, M.; Bartz, M.; Fomenko, A.; Tremel, W. *J. Appl. Crystallogr.* **2003**, *36*, 583−586.

(43) Mayya, K. S.; Caruso, F. *Langmuir* **2003**, *19*, 6987−6993.

(44) Bain, C. D.; Troughton, E. B.; Tao, Y.-T.; Evall, J.; Whitesides, G. M.; Nuzzo, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 321−335.

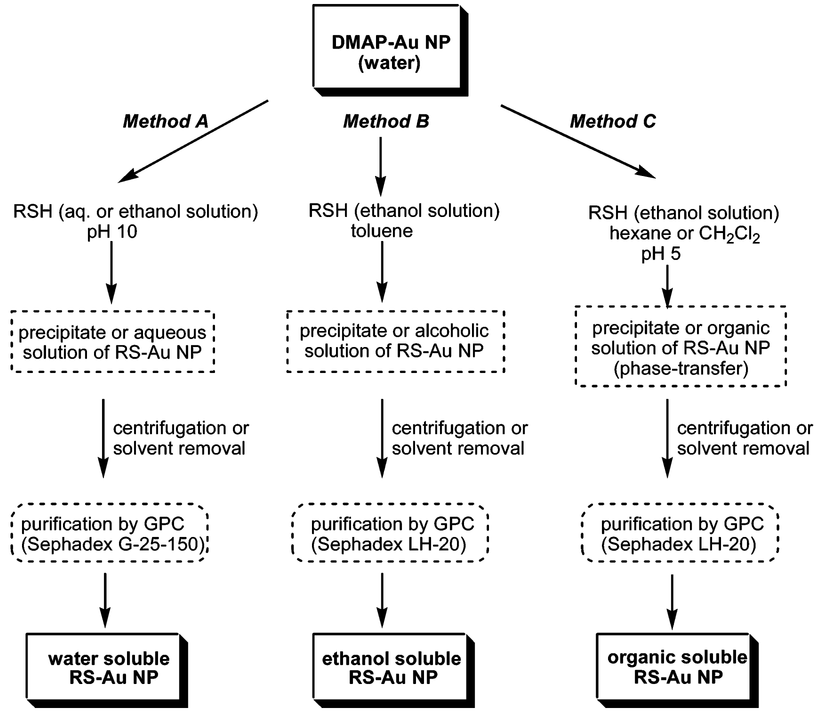
(45) Creager, S. E.; Rowe, G. K. *J. Electroanal. Chem.* **1994**, *370*, 203−211.

(46) Quist, F.; Tabard-Cossa, V.; Badia, A. *J. Phys. Chem. B* **2003**, *107*, 10691−10695.

(47) Gittins, D. I.; Caruso, F. *Angew. Chem., Int. Ed.* **2001**, *40*, 3001−3004.

(48) Gandubert, V. J.; Lennox, R. B. *Langmuir* **2005**, *21*, 6532−6539.

Chart 1. Water- and Organic-Soluble Au NP Prepared from Aqueous DMAP−Au NP



CM200 transmission electron microscope using an acceleration voltage of 200 kV. The 3 in. × 4 in. negatives were scanned at a resolution of 600 dpi using an Epson 1200 photo scanner and its negative adapter. For each sample, the mean diameter of the NP was determined using SigmaScan Pro5.0 software (SPSS Inc.), where ca. 200 particles constitute a data set per sample.

Thiol Area/Molecule Estimation. The number of alkylthiol ligands on the gold core can be reasonably determined by using TEM-derived areas when elemental analysis or TGA data are not available. The total gold surface of the NP is difficult to accurately estimate because of the complicated topology of Au NP. Two geometries have been considered: (faceted) truncated octahedron and sphere (refs 49 and 50 and references therein). With regard to the alkylthiol footprint, several values have been reported ranging from 15 to 21 Å^2.[26,49,51−53] This range arises because the surface density of alkylthiols is greater for small (<4 nm) than larger particles. We have opted to use a spherical geometry approximation and a median area/molecule of 18 Å^2 for simplicity. Given the number of assumptions and issues related to calculation of the thiol molecules required to fully cover the gold surface (stoichiometric quantity), this should be regarded as an estimated average.

***N,N,N*-Trimethyl(11-mercaptoundecyl)ammonium Bromide (BrMe$_3$NC$_{11}$SH).**[54] Trimethylamine was added (4 mL of solution 4.2 M in EtOH, 16.9 mmol) to a degassed solution of 11-bromoundecanethiol (3.48 g, 13 mmol) in ethyl acetate (20 mL). The solution turned orange-brown, and within 2 h a precipitate started to form. The reaction mixture was allowed to stir at room temperature under a stream of argon for 2 days. The white precipitate that resulted was removed by filtration, washed with EtOH and hexane (under a stream of argon), and dried in vacuo to yield the title product (2.3 g, isolated yield 53%). This product has similar spectroscopic properties to those reported previously for the ClMe$_3$NC$_{11}$SH.[55] ^{1}H NMR (400.128 MHz, D$_2$O) δ 1.27−1.42 (m, 14H, $-\mathrm{CH_{2-}}$), 1.53−1.61 (m, 2H, $-CH_2-\mathrm{CH_2}-\mathrm{SH}$), 1.71−1.79 (m, 2H, $-CH_2-\mathrm{CH_2}-\mathrm{NMe_3}$), 2.51 (t, J = 7.11 Hz, 2H, $-CH_2-\mathrm{SH}$), 3.07 (s, 9H, $-\mathrm{NMe_3}$), 3.26−3.30 (m, 2H, $-CH_2-\mathrm{NMe_3}$). ^{1}H NMR (400.128 MHz, CDCl$_3$) 1.27−1.36 (m, 14H, $-\mathrm{CH_{2-}}$), 1.58−1.63 (m, 2H, $-CH_2-\mathrm{CH_2}-\mathrm{SH}$), 1.71−1.78 (m, 2H, $-CH_2-\mathrm{CH_2}-\mathrm{NMe_3}$), 2.49−2.55 (m, 2H, $-CH_2-\mathrm{SH}$), 3.48 (s, 9H, $-\mathrm{NMe_3}$), 3.56−3.60 (m, 2H, $-CH_2-\mathrm{NMe_3}$). ES$^+$-MS *m*/*z* 246.3 (calcd average mass for C$_{14}$H$_{32}$NS$^+$: 246.23). HRMS *m*/*z* obsd 245.21819 (calcd 245.21772 for C$_{14}$H$_{31}$NS).

Synthesis of RS−Au NP from DMAP−Au NP via Place-Exchange Reactions. A thiol solution (in water or ethanol) is added to an aqueous solution of DMAP−Au NP at room temperature. Upon the ligand exchange the NP either precipitate, remain dissolved in the reaction mixture, or transfer into an organic phase (if present). Isolation and purification of the RS−Au NP are carried out according to one of the following workup pathways (Chart 1, Table 1).

Method A (Water-Soluble RS−Au NP). A volume of 30 mL of thiol solution (0.45 × 10^{-3} M in 95% ethanol, pH adjusted to 10 with a solution of 10% KOH) was added to a 20 mL aqueous solution of DMAP−Au NP. The solution becomes cloudy and changes color from dark-red to violet, then to violet−blue, as the ligand-exchange process proceeds when short-chain thiols and H$_2$NC$_{11}$SH are used. In the case of longer chain thiols as well as BrMe$_3$NC$_{11}$SH no changes in color or turbidity were observed. The mixture was left to stand at room temperature overnight. The dark precipitate (fine particles) was separated by gentle centrifugation, while the burgundy-red solution was carefully evaporated under reduced pressure (bath temperature 30−35 °C). The precipitate/solid residue was then dissolved in the minimum volume of Milli-Q

---

(49) Badia, A.; Cuccia, L.; Demers, L.; Morin, F.; Lennox, R. B. *J. Am. Chem. Soc.* **1997**, *119*, 2682−2692.

(50) Corbierre, M. K.; Cameron, N. S.; Lennox, R. B. *Langmuir* **2004**, *20*, 2867−2873.

(51) Badia, A.; Singh, S.; Demers, L.; Cuccia, L.; Brown, G. R.; Lennox, R. B. *Chem. Eur. J.* **1996**, *2*, 359−363.

(52) Kimura, K.; Takashima, S.; Ohshima, H. *J. Phys. Chem. B* **2002**, *106*, 7260−7266.

(53) Yamada, M.; Nishihara, H. *C. R. Chim.* **2003**, *6*, 919−934.

(54) Lana, I. J.; Abbott, N. L. *Langmuir* **1998**, *14*, 2235−2237.

(55) Tien, J.; Terfort, A.; Whitesides, G. M. *Langmuir* **1997**, *13*, 5349−5355.

Table 1. Description of the RS−Au NP Prepared by Ligand-Exchange from DMAP−Au NP

ligand	method	stability: solution	stability: solid state	characteristics: λ_{max} (nm)	characteristics: mean core diam (nm)[a]
DMAP	ref 47	yes	no	520 (H_2O, pH 10)	4.9 ± 0.9
$HOOCC_2SH$	A	yes	no	514 (H_2O, pH 9)	4.5 ± 1.0
$HOOCC_{10}SH$	A	yes	yes	515 (H_2O, pH 9)	4.0 ± 0.8
$HOOCC_{15}SH$	A	yes	yes	522 (H_2O, pH 9)	4.6 ± 1.0
thioctic acid	A	yes	yes	515 (H_2O, pH 9)	4.6 ± 1.0
H_2NC_2SH	A	yes	no	519 (H_2O, pH 3)	4.4 ± 1.0
$H_2NC_{11}SH$	A	yes	yes	520 (H_2O, pH 3)	4.7 ± 0.8
Me_2NC_2SH	A	limited[b]	no	514 (H_2O, pH 3)	4.4 ± 1.0
$BrMe_3NC_{11}SH$	A	yes	yes	517 (H_2O, pH 7)	5.4 ± 1.0
$HOC_{11}SH$	B	yes	yes	519 (EtOH/H_2O 1:1)	4.6 ± 0.9
$HOC_{14}SH$	B	yes	yes	519 (EtOH)	4.3 ± 0.7
$C_{10}SH$	C	yes	yes	516 (CH_2Cl_2), (toluene) 519	4.2 ± 0.7
$FcC_{12}SH$	C	yes	yes	517 (CH_2Cl_2), (toluene) 519	4.1 ± 0.6
$BrC_{11}SH$	C	yes	yes	518 (CH_2Cl_2), (toluene) 520	4.4 ± 1.0

[a] Obtained from TEM measurements of 200−400 NP per sample. [b] Stable for hours to days after GPC purification, stable for longer periods if less pure.

water at basic pH (9−10; 10% KOH) for $-NH_2$ and $-NMe_2$-functionalized NP, acidic pH (3−4; 20% acetic acid) for −COOH-functionalized NP, and neutral pH for $BrMe_3N$-derivatized NP. The resulting solution was loaded onto a Sephadex G-25−150 column and eluted with Milli-Q water (pH = 9−10, 3−4, 7, respectively). The dark-red fraction was collected. Samples for ^1H NMR measurements were prepared by freeze-drying and redissolution in D_2O at pH 3−4 (CD_3COOD) or 9−10 (KOH). The freeze-drying has to be stopped before it reaches completion in the short-chain thiol case, because these NP are not stable when dried.

Method B (Ethanol-Soluble RS−Au NP). A volume of 30 mL of a thiol solution (0.45×10^{-3} M in 95% ethanol) was added to a 20 mL of aqueous solution of DMAP−Au NP, followed by 30 mL of toluene. The solution became cloudy and changed from dark-red to violet in the case of $HOC_{11}SH$ and remained clear burgundy-red for the case of $HOC_{14}SH$. The reaction mixture was left to stand at room temperature overnight. The $HOC_{11}S$−Au precipitate was isolated by centrifugation and taken up in a minimum volume of EtOH/water (4:1). The clear red $HOC_{14}S$−Au solution was rotary evaporated, and the reddish solid was redispersed in the minimum volume of EtOH/water (4:1). Purification on a Sephadex LH-20 column (elution with EtOH/water, 4:1) yields the HO-functionalized NP as a concentrated dark-red solution that can be stored as is or dried under reduced pressure (rotary evaporator).

Method C (Organic-Soluble RS−Au NP). To a 20 mL aqueous solution of DMAP−Au NP, 30 mL of a thiol solution (0.45×10^{-3} M in 95% ethanol) was added, followed by 20 mL of organic solvent (hexane or CH_2Cl_2). For the thiols less soluble in ethanol (i.e., $FcC_{12}SH$) the solution was prepared by dilution from a stock solution in CH_2Cl_2 or CH_2Cl_2/EtOH 4:1. When CH_2Cl_2 was used, additional solvent or water was added in order to separate the two phases because of the CH_2Cl_2–EtOH miscibility. The pH of the reaction mixture was reduced to 5 by addition of HOAc (20%). The aqueous phase becomes cloudy and changes color from dark-red to violet to colorless as newly formed NP transfer into the organic layer. The phase-transfer process is complete within a few minutes. When CH_2Cl_2 is used the newly formed NP precipitate because of the residual EtOH. In the case of hexane, the NP remain disperse in the organic layer. The reaction mixture was left to stand at room temperature overnight. The workup procedure depends on the solvent used. The precipitate was isolated by gentle centrifugation and taken up in a minimum volume of CH_2Cl_2. The clear red solution was reduced to dryness, and the reddish solid was redissolved in a minimum volume of CH_2Cl_2. Further purification was achieved by GPC (Sephadex LH-20) using CH_2Cl_2/hexane/MeOH (75:25:10) as eluting solvent. The dark-red moving band was collected and dried under reduced pressure. Depending on the column load, sometimes a second column purification is necessary. The Sephadex was reused after appropriate solvent washing.

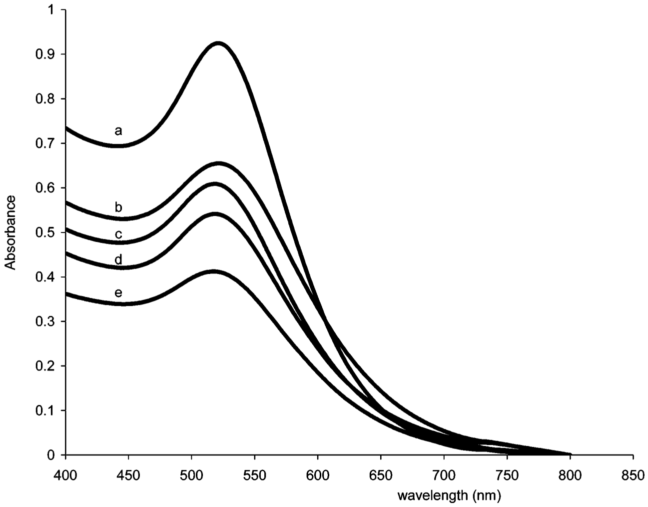


Figure 1. UV−vis spectra of Au NP prepared by place-exchange reaction from DMAP−Au: (a) DMAP−Au NP; (b) $HOC_{11}S$−Au NP; (c) $BrC_{11}S$−Au NP; (d) H_2NC_2S−Au NP; (e) $FcC_{12}S$−Au NP.

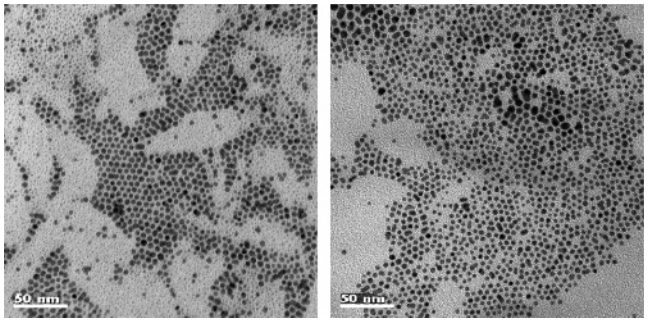


Figure 2. TEM images of $C_{10}S$−Au NP (left) and DMAP−Au NP (right). The scale bar represents 50 nm.

NP Characterization. All NP prepared have been characterized by ^1H NMR, UV−vis spectroscopy, and TEM. The NMR and MS spectra show that DMAP, excess thiols, and residual gold salts have been efficiently removed by gel permeation chromatography (see the Supporting Information). The small shifts in the plasmon absorption (ranging between 514 and 522 nm) with respect to the DMAP−Au NP (520 nm) (Figure 1) are due to (i) the change in the refractive index upon phase-transfer from water (1.33) to dichloromethane (1.4242) or toluene (1.4961)[43,56] and/or (ii) the formation of a low-dielectric layer around the colloidal metal.[57] TEM images (Figures 2 and 3) are consistent with the UV−vis data and prove that the size of the initial DMAP−Au NP is preserved in both water- and organic-soluble NP prepared.

Results and Discussion

DMAP−Au NP prepared from toluene-soluble TOAB−Au NP by a ligand-exchange approach have several attractive properties. They are (i) quite monodisperse, (ii) exhibit

---

(56) Thomas, K. G.; Zajicek, J.; Kamat, P. V. *Langmuir* **2002**, *18*, 3722−3727.

(57) Aslan, K.; Perez-Luna, V. H. *Langmuir* **2002**, *18*, 6059−6065.

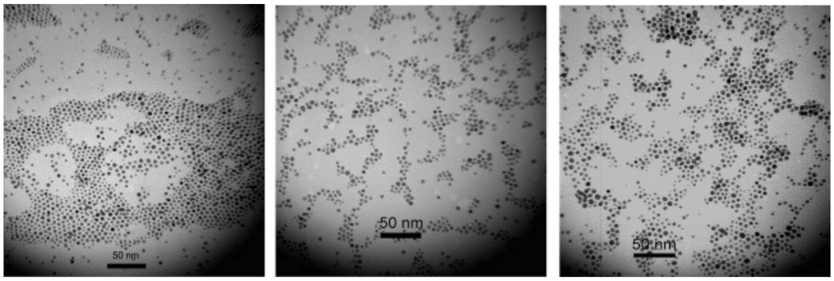


Figure 3. TEM images of $FcC_{12}S-Au$ NP (left), $HOC_{14}S-Au$ NP (center), and $H_2NC_{11}S-Au$ NP (right).

excellent stability in solution (pH ≈ 10) over long periods of time (samples have been kept at 4 °C for more than 2 years with no sign of degradation), (iii) exhibit stability over a broad pH range (5−12),[48] and (iv) are available as a highly concentrated aqueous solution. These features make DMAP−Au NP attractive as precursors for a range of functionalized gold NP (Scheme 1, Chart 1, and Table 1).

Organic-Soluble NP. *n*-Decanethiol is very frequently used as a stabilizing agent for gold NP.[58−60] Because it does not possess functional groups that might interfere in the place-exchange process, it had been used to prepare RS−Au NP by the thiol-for-thiol place-exchange reaction.[21,61] The exchange process described here is readily monitored because DMAP replacement is accompanied by the phase-transfer of the NP from water into the organic layer. Experiments performed with a large excess of $C_{10}SH$ (0.1 M in EtOH), equivalent to 160 monolayers/particle (estimated by assuming that the occupied surface area by a single thiol molecule is 18 $Å^2$), lead to a very rapid ligand-exchange reaction. No precipitate forms, and the NP transferred into the organic phase display the burgundy-red color of DMAP−Au NP. This establishes that little or no aggregation has occurred, because the aggregation process is usually manifested by formation of an insoluble precipitate and/or a change in color due to the red-shift of the surface plasmon absorption peak.[61] Both TLC and the ^1H NMR spectrum indicate that some DMAP also transfers into the organic phase. Because the pH of the DMAP−Au NP solution is near the DMAP pK_a (10 compare to 9.7), a distribution of DMAP between the aqueous and organic layers results.[48] Residual DMAP is readily removed by washing the $C_{10}S-Au$ NP toluene solution with acidic water (pH 5, monitored by TLC and ^1H NMR), with no degradation of $C_{10}S-Au$ NP. TEM analysis of the isolated $C_{10}S-Au$ NP shows that the size and narrow dispersity of the DMAP−Au precursor is preserved (Figure 2). Residual DMAP is thus much more easily removed than is residual thiol, as the latter requires serial precipitations and washings with EtOH. Such repetitive precipitations result in a significant loss of NP. Lesser quantities of thiol (corresponding to 40 and 75 monolayers/particle) facilitate the purification step but lead to significant NP aggregation. Because the DMAP−Au NP solution contains a considerable quantity of free DMAP (necessary because of the equilibrium between gold-bound and free DMAP),[34,47,48] it is possible that the free DMAP competes with the thiol and impedes the ligand-exchange process. Nevertheless, the place-exchange process is promoted by adjusting the pH to 5 so that most of the free DMAP is protonated and thus not capable of binding to the gold surface.[48] A gradual decrease of the pH to 5 after addition of the thiol leads to efficient place-exchange even with stoichiometric amounts of thiol, with no apparent aggregation occurring. The purification step is also facilitated as most of the DMAP remains in the aqueous phase. Residual DMAP and thiol were efficiently removed by gel permeation chromatography (Sephadex)[33] yielding pure NP.

This procedure was successfully extended to other thiol-capped NP, which until now have only been available as mixed monolayers. For example, ferrocene-derivatized Au NP have been prepared via this method. These NP are particularly interesting for electrochemical applications.[62,63] Ferrocene moieties have been previously introduced into the protective layer by place-exchange reactions using as starting materials thiolate-,[16,18,19,53,62−65] or citrate-protected Au NP,[66,67] or Au NP/streptavidin conjugates.[68,69] These procedures lead to mixed alkylthiol/ferrocenylthiol monolayers. A complex citrate−Au NP approach uses α-cyclodextrin to transfer the ferrocenylthiol to the aqueous phase.[70] The only direct synthesis leading to homogeneous capping layers reported to date uses 4-ferrocenylthiophenol but not ferrocenylalkylthiols.[71] The procedure developed in this study leads to a complete $FcC_{12}SH$ capping layer on the NP (Table 1, Figure 3). Another important capping ligand is $BrC_{11}SH$. Attempts to prepare $BrC_{11}S-Au$ NP using the Ulman procedure have been unsuccessful[72] as the terminal $-CH_2Br$ functions are

---

(58) Han, L.; Maye, M. M.; Leibowitz, F. L.; Ly, N. K.; Zhong, C.-J. *J. Mater. Chem.* **2001**, *11*, 1258−1264.

(59) Kariuki, N. N.; Han, L.; Ly, N. K.; Patterson, M. J.; Maye, M. M.; Liu, G.; Zhong, C.-J. *Langmuir* **2002**, *18*, 8255−8259.

(60) Shelley, E. J.; Ryan, D.; Johnson, S. R.; Couillard, M.; Fitzmaurice, D.; Nellist, P. D.; Chen, Y.; Palmer, R. E.; Preece, J. A. *Langmuir* **2002**, *18*, 1791−1795.

(61) Weisbecker, C. S.; Merritt, M. V.; Whitesides, G. M. *Langmuir* **1996**, *12*, 3763−3772.

(62) Green, S. J.; Stokes, J. J.; Hostetler, M. J.; Pietron, J.; Murray, R. W. *J. Phys. Chem. B* **1997**, *101*, 2663−2668.

(63) Chen, S. *Langmuir* **2001**, *17*, 6664−6668.

(64) Labande, A.; Ruiz, J.; Astruc, D. *J. Am. Chem. Soc.* **2002**, *124*, 1782−1789.

(65) Daniel, M.-C.; Ruiz, J.; Nlate, S.; Blais, J.-C.; Astruc, D. *J. Am. Chem. Soc.* **2003**, *125*, 2617−2628.

(66) Peng, Z.; Qu, X.; Dong, S. *Langmuir* **2004**, *20*, 5−10.

(67) Qu, X.; Peng, Z.; Jiang, X.; Dong, S. *Langmuir* **2004**, *20*, 2519−2522.

(68) Wang, J.; Li, J.; Baca, A. J.; Hu, J.; Zhou, F.; Yan, W.; Pang, D.-W. *Anal. Chem.* **2003**, *75*, 3941−3945.

(69) Baca, A. J.; Zhou, F.; Wang, J.; Hu, J.; Li, J.; Wang, J.; Chikneyan, Z. S. *Electroanalysis* **2004**, *16*, 73−80.

(70) Liu, J.; Xu, R.; Kaifer, A. E. *Langmuir* **1998**, *14*, 7337−7339.

(71) Li, D.; Zhang, Y.; Jiang, J.; Li, J. *J. Colloid Interface Sci.* **2003**, *264*, 109−113.

(72) Rusa, M.; Whitesell, J. K.; Fox, M. A. *Macromolecules* **2004**, *37*, 2766−2774.

reduced to $-CH_3$ by the Superhydride. The one-phase reaction[72] on the other hand offers poor control over the NP size distribution (2−4 nm), and the thiol-for-thiol exchange leads to a mixed alkanethiolate/bromododecanethiol layer.[18] $BrC_{11}S-Au$ NP prepared using a DMAP−Au NP precursor are stable in the solid state and can be repeatedly dissolved in organic solvents (CH_2Cl_2 or hexane) without obvious degradation. Hydroxy-terminated thiols are very attractive targets as they are potential precursors to ether or ester derivatives. However, the preparation and isolation of HOC_nS-Au NP is problematic. $HOC_{11}S-Au$ NP are not accessible via the Ulman reaction.[72] Mixed-layers NP have previously been prepared either by the Brust−Schiffrin[73] or place-exchange reactions.[74,75] Small $HOC_{16}S-Au$ NP have been prepared by the two-phase synthesis but are insoluble in common NMR solvents.[76] $HOC_{11}S-Au$ NP were recently reported to be available by a two-phase procedure, but there is no mention about their solubility and stability.[77] While this work was in progress, HOC_6S-Au NP were reported from TOAB−Au NP, but the isolation and purification steps are lengthy and tedious.[78] Stable, soluble $HOC_{11}S-Au$ NP are in fact readily accessible via DMAP−Au NP (Table 1). Interestingly, these NP are not soluble in absolute ethanol but are soluble in dilute ethanol (40−80%). They are also stable in the solid state (dark-reddish powder) and in solution (several months). Similarly prepared $HOC_{14}S-Au$ NP are soluble in MeOH and EtOH (absolute) (Table 1 and Figure 3).

Water-Soluble NP. Water-soluble gold NP are of interest due to the large spectrum of applications varying from biolabeling to drug delivery systems. Ionizable groups such as $-NH_2$, $-NMe_2$, or $-COOH$ attached to the pendant chains are of interest for their water solubility and coupling reactions. However, such NP are still a synthetic challenge. A recent systematic overview summarized the limitations associated with the preparation of water-soluble gold NP by the Brust−Schiffrin procedure.[79]

An adaptation of the DMAP−Au NP-based procedure accommodates the fact that both precursor and product NP are water-soluble (see the Experimental Section). NP stabilized with short-chain thiols ($HOOCC_2S-Au$, H_2NC_2S-Au, Me_2NC_2S-Au) undergo irreversible aggregation in the solid state. Upon complete removal of water NP aggregate probably due to interparticle binding via H-bonds. Samples required for NMR measurements were prepared by freeze-drying, but care has to be taken to prevent complete removal of water. As long as there remains a small amount of water these NP can be readily redissolved in water. NP capped with acid-terminated thiols are more stable toward aggregation than those stabilized with base-terminated thiols (HOOC-functionalized NP vs H_2N- and Me_2N-functionalized NP). $HOOCC_2S-Au$ are stable for months, NH_2C_2S-Au NP are stable up to 5−6 weeks, and Me_2NC_2S-Au are stable for several hours or days. The differences in stability toward aggregation are not understood yet, but it has been reported that small H_2NC_2S-Au NP (mean diameter < 2 nm) eventually form much larger NP (mean diameter 33 nm).[80] The extent of the purification seems to affect the H_2N- and Me_2N-terminated Au NP stability. Batches of Me_2NC_2S-Au NP purified by repetitive toluene washing instead of GPC proved to be stable in solution for more than 1 year. The toluene extraction readily removes the DMAP (at pH 10) but not the residual thiol. Samples purified by gel permeation chromatography, where all free thiol is removed, are stable only for hours or several days.

Small (1.5 nm) gold NP capped with short-chain ($-C_2H_{4-}$) thiols bearing $-COOH$, $-NMe_2$, $-NMe_3Cl$, and $-SO_3Na$ groups have been recently reported by Woehrle et al.[33] These NP are prepared from triphenylphosphine−Au NP by a ligand-exchange reaction and are stable both in solution and solid state.[33] Previous attempts to stabilize large NP (17 and 40 nm) with short-chain thiols gave unsatisfactory results as flocculation occurred.[28,61] The short-chain thiol-capped Au NP prepared during the present study are of an intermediate size (4−5 nm). Short-chain thiols are known as being weak stabilizers for Au NP, especially those soluble in organic solvents (ref 79 and references therein). Unlike their short-chain counterparts, long-chain alkylthiols (C_{10} to C_{15}) impart much better stability to Au NP.[79] Consequently, $H_2NC_{11}SH$-capped NP are readily prepared from the DMAP−Au precursor and are stable in the solid state (Figure 3). Redissolution in acidic water is slow (10−12 h) but complete. $HOOCC_{11}SH$ and $HOOCC_{15}SH$ also readily displace the DMAP capping layer, forming very stable NP both in solution and the solid state.

Since the alkylthiol-capped Au NP solubility in water is determined by the terminal groups in the case of carboxyl- and amine-functionalized NP, their solubility is pH-dependent. To gain a broader, usable pH range we investigated Au NP stabilized with quaternary ammonium-terminated thiols. For example, $BrMe_3NC_{11}S-Au$ NP are very stable in solution and the solid state. They are also stable in solution over the entire pH range ($1 < pH < 14$) for up to 2 months. Ammonium-terminated NP have been previously prepared by place-exchange reactions from C_8S-Au NP (mixed monolayers; 2 nm)[81] and by direct synthesis in water (4.4 nm).[82]

Another important capping agent is 6,8-thioctic acid (lipoic acid), which was previously used as an intermediate to prepare mixed thiol-capped Au NP starting from citrate−Au NP.[28] Thioctic acid−Au NP with a mean diameter about 5 nm have been recently prepared by one-phase

---

(73) Shon, Y.-S.; Mazzitelli, C.; Murray, R. W. *Langmuir* **2001**, *17*, 7735−7741.

(74) Norgaard, K.; Weygand, M. J.; Kjaer, K.; Brust, M.; Bjornholm, T. *Faraday Discuss.* **2004**, *125*, 221−233.

(75) Yin, H.-Z.; Liu, H.; Li, Y.-Y.; He, X.-W.; Chen, L.-X.; Li, W.-Y. *Huaxue Xuebao* **2005**, *63*, 734−738.

(76) Badia, A.; Gao, W.; Singh, S.; Demers, L.; Cuccia, L.; Reven, L. *Langmuir* **1996**, *12*, 1262−1269.

(77) Belser, T.; Stohr, M.; Pfaltz, A. *J. Am. Chem. Soc.* **2005**, *127*, 8720−8731.

(78) Wanunu, M.; Popovitz-Biro, R.; Cohen, H.; Vaskevich, A.; Rubinstein, I. *J. Am. Chem. Soc.* **2005**, *127*, 9207−9215.

(79) Ackerson, C. J.; Jadzinsky, P. D.; Kornberg, R. D. *J. Am. Chem. Soc.* **2005**, *127*, 6550−6551.

(80) Niidome, T.; Nakashima, K.; Takahashi, H.; Niidome, Y. *Chem. Commun.* **2004**, 1978−1979.

(81) McIntosh, C. M.; Esposito, E. A., III; Boal, A. K.; Simard, J. M.; Martin, C. T.; Rotello, V. M. *J. Am. Chem. Soc.* **2001**, *123*, 7626−7629.

(82) Cliffel, D. E.; Zamborini, F. P.; Gross, S. M.; Murray, R. W. *Langmuir* **2000**, *16*, 9699−9702.

synthesis.[83] However, this procedure requires the use of the dihydrolipoic acid, the reduced form of thioctic acid, to avoid a competition between the reduction of gold salt and thioctic acid.[83] Recently, Abad et al. have prepared thioctic acid-capped NP with a mean diameter of 3 nm NP by place-exchange reaction from TOAB−Au NP.[84] However, this approach uses a larger amount of thiol than that used in the DMAP−Au procedure and the purification step requires repetitive toluene/alcohol washings. Thioctic acid-stabilized Au NP are easily accessible via the DMAP−Au NP route. Thioctic acid-stabilized Au NP prepared from the DMAP−Au precursor exhibit excellent stability both in solution (pH 8−10) and the solid state.

Comparison to TOAB−Au NP as a Starting Material. Although TOAB is used as a phase-transfer reagent in the Brust−Schiffrin two-phase reaction, it also can serve as a capping agent.[85] Several water-soluble Au NP have been previously prepared by exchanging TOAB with DMAP,[43,47] $HOOCC_{11}SH$, 4-carboxy-thiophenol,[43] and more recently thioctic acid[84] and HOC_6SH.[78] We have also tested thiols such as $C_{10}SH$, $BrC_{11}SH$, and $FcCH_{12}SH$ (used as solutions in ethanol) in thiol-for-TOAB exchange reactions. Although stable NP are obtained, the purification step proves to be difficult due to the presence of residual TOAB. TOAB is difficult to completely remove even after repetitive purification by gel permeation chromatography. Previous reports indicate that residual TOAB is retained in the thiol-capped NP, and Soxhlet extraction with acetone is needed in order to remove it.[10,11] Moreover, attempts to replace the TOAB by short-chain thiols ($HOOCC_2SH$, H_2NC_2SH, Me_2NC_2SH) yield insoluble precipitates or very unstable NP even when a large excess of thiol is used. TOAB−Au NP thus seem to be of limited use in the preparation of the thiol-capped NP.

Overview and Conclusions

A new procedure to prepare ligand-capped water- and organic-soluble Au NP in the range of 4−6 nm has been developed using DMAP−Au NP as a starting material. The stability conferred by the thiol chain length and/or terminal functions, finely controlled solubility via the peripheral groups, and selective affinity of gold for different ligands (thiols > DMAP) make the thiol-for-DMAP exchange reaction an attractive synthetic route. DMAP is readily and efficiently displaced by a variety of functionalized thiols under mild conditions (room temperature, ambient atmosphere). The procedure developed has the advantage of needing only stoichiometric quantities of thiol, whereas other procedures require a large excess of incoming thiol. This is important when rare and expensive thiols are needed to be introduced in the protective layer. DMAP−Au NP can also be used to prepare Au NP protected with thiols bearing functions incompatible with the reductive conditions associated with $NaBH_4$ or superhydride. Unlike thiol-for-thiol exchange reactions, the present method offers control over the composition of the final products. This feature is important when further chemical modification of the capping layer is of interest. The procedure is straightforward and offers access to a broad range of Au NP.

Acknowledgment. The authors thank Dr. Xue-Dong Liu of McGill University, Physics Department for the TEM imaging. Mass spectrometry measurements were kindly performed by Nadim Saadeh. Dr. Muriel K. Corbierre is acknowledged for help with the truncated octahedron model and Adil Kassam for valuable and insightful discussions on gold NP preparation and purification. This research was supported by NSERC and FQRNT.

Supporting Information Available: ^1H NMR, UV−vis spectra, and TEM pictures of all NP prepared by place-exchange reactions from DMAP−Au precursors. This material is available free of charge via the Internet at http://pubs.acs.org.

CM060793+

---

(83) Roux, S.; Garcia, B.; Bridot, J.-L.; Salome, M.; Marquette, C.; Lemelle, L.; Gillet, P.; Blum, L.; Perriat, P.; Tillement, O. *Langmuir* **2005**, *21*, 2526−2536.

(84) Abad, J. M.; Mertens, S. F. L.; Pita, M.; Fernandez, V. M.; Schiffrin, D. J. *J. Am. Chem. Soc.* **2005**, *127*, 5689−5694.

(85) Brust, M.; Bethell, D.; Schiffrin, D. J.; Kiely, C. J. *Adv. Mater.* **1995**, *7*, 795−797.