

# Formation and pH-controlled assembly of amphiphilic gold nanoparticles

Joseph Simard, Cheryl Briggs, Andrew K. Boal and Vincent M. Rotello\*

Department of Chemistry, University of Massachusetts, Amherst, MA 01003, USA. E-mail: rotello@chem.umass.edu

Received (in Columbia, MO, USA) 23rd May 2000, Accepted 16th August 2000

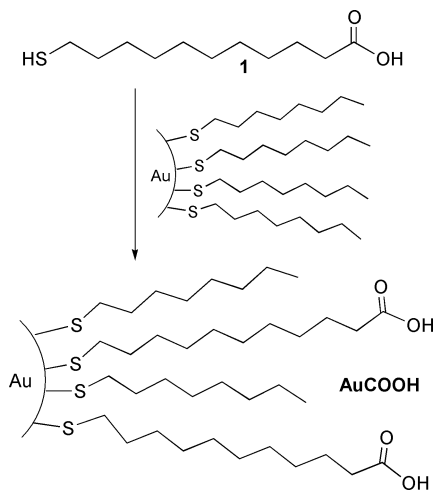
First published as an Advance Article on the web

**Alkanethiolate-protected gold nanoclusters are solubilized through place exchange reaction with  $\omega$ -thiocarboxylic acids.**

Thiolate monolayer-protected gold clusters (MPCs) provide versatile precursors for the fabrication of nanoscale systems.<sup>1</sup> These colloidal MPCs can be readily modified through place exchange reactions,<sup>2</sup> providing a direct route to mixed monolayer-protected clusters (MMPCs) featuring a broad array of functionality. This functional diversity, coupled with the combinatorial nature of the place exchange process, has made MMPCs central in the creation of numerous nanoparticle-based materials and devices.

One potentially powerful application of MMPCs is biomolecular recognition.<sup>3</sup> In recent investigations, we have demonstrated that the mobility of thiolate ligands on nanoparticles can be exploited to create templated multivalent receptors.<sup>4</sup> The extension of this methodology to the recognition of protein surfaces<sup>5</sup> has been limited by the inaccessibility of water-soluble amphiphilic MMPCs. Recently, Murray and co-workers have demonstrated the formation of water-soluble MPCs and place exchange reactions to produce the corresponding MMPCs.<sup>6</sup> In both the colloid formation and place exchange steps, however, purification of the resulting colloids required lengthy dialysis to remove unreacted thiols. More significantly, attempts to exchange hydrophobic groups into water-soluble MPCs resulted in the formation of insoluble aggregates.<sup>6c</sup> To provide an alternative route to the formation of amphiphilic colloids we have explored the exchange of polar functionality with gold nanoparticles featuring non-polar monolayer coverage. We report here the direct formation of water-soluble amphiphilic colloids through place exchange of alkanethiolate MPCs with an  $\omega$ -thiol carboxylic acid.

To obtain a system that would provide water solubility with non-polar groups present, we prepared the carboxylic acid-functionalized colloid AuCOOH through place exchange of 2 nm octanethiol colloids<sup>7</sup> with 11-thioundecanoic acid **1** (Scheme 1).<sup>8</sup> After washing with dichloromethane, the AuCOOH nanoparticles were dissolved in D<sub>2</sub>O/NaOD, and

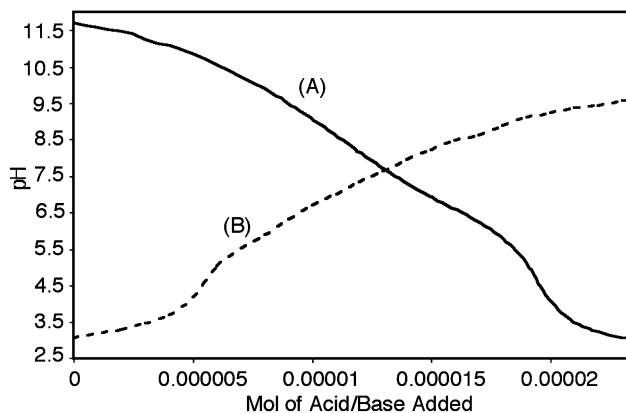


Scheme 1

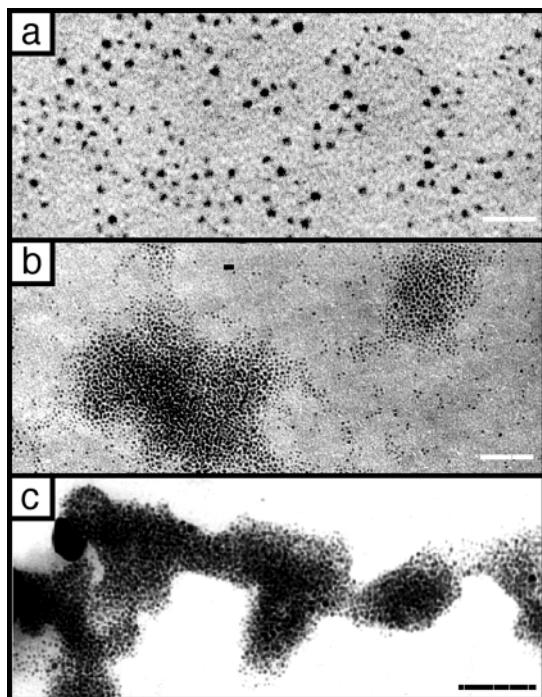
characterized by NMR. The end-group analysis of the <sup>1</sup>H NMR spectrum of the resulting AuCOO<sup>-</sup> colloids indicated that the ratio of  $\omega$ -thiol carboxylic acid to octanethiol was *ca.* 1:1.

The functionalized colloids were also characterized by pH titration. Acid/base titrations of nanoparticles with ionizable monolayer moieties have been carried out previously.<sup>6c,9</sup> Fig. 1A shows the titration of AuCOO<sup>-</sup>, which exhibited a pK<sub>a</sub> of about 4.0. This corresponds closely to previous work done on carboxylate-terminated MPCs featuring a C<sub>12</sub> monolayer, where a pK<sub>a</sub> of 4.5 was reported,<sup>8</sup> and is considerably lower than the pK<sub>a</sub> of 5.56 observed with tipronin (C<sub>4</sub>)-functionalized MPCs. This disparity in pH provides further evidence of the distance dependence of sidechain–sidechain interactions arising from the radial nature of MPC systems.<sup>10</sup>

During titrations, aggregation of particles was observed at pH < 5. This is attributed to interparticle interactions: at low pH the carboxylic acid groups facilitate interparticle interactions through both hydrogen bonding and an increase in hydrophobicity, resulting in the formation of particle aggregates. At high pH, however, particle aggregation is disfavored due to repulsive interactions between negatively charged carboxylate particles.<sup>11</sup> Transmission electron microscopy (TEM) was used to better understand the aggregation process.<sup>8,9</sup> Samples were prepared by initially dissolving AuCOOH nanoparticles in pH 10 buffer. A portion of this solution was neutralized to pH ~ 7 with 0.1 M HCl which was then diluted with pH 7 or pH 4 buffer, producing three solutions with pH 10, 7, and 4. All the solutions were diluted with sufficient buffer to yield a final colloid concentration of 1 mg mL<sup>-1</sup>. A single drop of the desired solution was deposited on a TEM grid.<sup>12</sup> At pH 10, there was very little aggregation, as would be expected for a highly charged colloid (Fig. 2a). When this system was deposited from a neutral pH 7 solution (Fig. 2b) both small loosely packed aggregates and individual particles were observed. At pH 4, (Fig. 2c), aggregation was increased, with very few free particles observed. Additionally, these aggregates are much larger and denser than those observed at pH 7.



**Fig. 1** Titration curves of AuCOOH. The colloid was first dissolved in a small amount of 0.1 M NaOH and brought up to a volume of 3.3 ml with distilled water. (A) Original solution titrated with aliquots of 10–50  $\mu$ L 0.01 M HCl. (B) Back titration of solution. Titrated with aliquots of 10  $\mu$ L 0.1 M NaOH. The pH was recorded initially and after each addition of either the acid or base.



**Fig. 2** TEM micrographs of  $\omega$ -thiol carboxylic acid functionalized colloid at (a) pH 10, (b) pH 7, and (c) pH 4. Scale bars represent 10 nm, 25 nm, and 50 nm, respectively.

In summary, we have demonstrated the effective fabrication of a water-soluble amphiphilic MMPC through place-exchange processes. We have also shown that aggregation of these particles can be directly controlled through modulation of pH. The application of these water-soluble MMPCs to molecular and biomolecular recognition is currently underway, and will be reported in due course.

This research was supported by the National Science Foundation (CHE 9905492 to V. M. R.; DMR-9809365 for MRSEC instrumentation), and the National Institutes of Health (GM-59249). V. M. R. acknowledges the Petroleum Research Fund of the ACS, the Alfred P. Sloan Foundation, the Camille

and Henry Dreyfus Foundation, and is a Cottrell scholar of Research Corporation.

## Notes and references

- 1 J. Liu, R. L. Xu and A. E. Kaifer, *Langmuir*, 1998, **14**, 7337.
- 2 M. J. Hostetler, A. C. Templeton and R. W. Murray, *Langmuir*, 1999, **15**, 3782.
- 3 A. P. Alivisatos, K. P. Johnsson, X. G. Peng, T. E. Wilson, C. J. Loweth, M. P. Bruchez and P. G. Schultz, *Nature*, 1996, **382**, 609; B. Johnne, K. Hansen, E. Mork and J. Holtlund, *J. Immunol. Methods*, 1995, **183**, 167; C. A. Mirkin, R. L. Letsinger, R. C. Mucic and J. J. Storhoff, *Nature*, 1996, **382**, 607; G. P. Mitchell, C. A. Mirkin and R. L. Letsinger, *J. Am. Chem. Soc.*, 1999, **121**, 8122; O. D. Velev and E. W. Kaler, *Langmuir*, 1999, **15**, 3693.
- 4 A. K. Boal and V. M. Rotello, *J. Am. Chem. Soc.*, 2000, **122**, 734.
- 5 For recent examples of protein surface recognition using other synthetic scaffolds, see: H. S. Park, Q. Lin and A. D. Hamilton, *J. Am. Chem. Soc.*, 1999, **121**, 8; L. E. Strong and L. L. Kiessling, *J. Am. Chem. Soc.*, 1999, **121**, 6193.
- 6 (a) A. C. Templeton, M. J. Hostetler, E. K. Warmoth, S. W. Chen, C. M. Hartshorn, V. M. Krishnamurthy, M. D. E. Forbes and R. W. Murray, *J. Am. Chem. Soc.*, 1998, **120**, 4845; (b) A. C. Templeton, D. E. Cliffel and R. W. Murray, *J. Am. Chem. Soc.*, 1999, **121**, 7081; (c) A. C. Templeton, S. W. Chen, S. M. Gross and R. W. Murray, *Langmuir*, 1999, **15**, 66.
- 7 D. G. Duff, A. Baiker and P. P. Edwards, *J. Chem. Soc., Chem. Commun.*, 1993, 96.
- 8 In a typical procedure, 11-thioundecanoic acid (740 mg, 3.4 mmol) in 4 mL of THF was added to 140 mg of  $C_8$ -functionalized nanoparticles.<sup>4</sup> The resulting solution was stirred under argon for two days at room temperature, forming a black precipitate of AuCOOH. Solvent was removed *in vacuo*, and the resulting solid purified by repeated suspension, centrifugation, and decanting with dichloromethane. The resulting AuCOOH colloid was soluble in polar organic solvents such as methanol, and ethanol, and slightly soluble in THF. Solubilization of AuCOOH colloid aqueous solution was achieved using aqueous solution at pH 10. This solution of AuCOOH could be acidified to pH ~ 5 before precipitation occurred.
- 9 C. S. Weisbecker, M. V. Merritt and G. M. Whitesides, *Langmuir*, 1996, **12**, 3763.
- 10 A. C. Templeton, M. P. Wuelfing and R. W. Murray, *Acc. Chem. Res.*, 2000, **33**, 27.
- 11 S. H. Chen and K. Kimura, *Langmuir*, 1999, **15**, 1075.
- 12 The samples were analyzed using a JEOL 100CX electron microscope, on 300 mesh Cu grid with carbon film.