Reliable stabilization and functionalization of nanoparticles through tridentate thiolate ligands†

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Novel amphiphilic trithiolates possess excellent properties for gold nanoparticle (AuNP) stabilization and functionalization and cannot be replaced by exchange reactions.

The connection of molecular recognition and solid state properties in homogeneous solution is the challenge of nanoparticle research today. In modern applications like single molecule detection and manipulation, the nanoparticle and the molecular component have to form an individual unit. For this purpose it is essential to get insight not only into physical properties of the particle core (magnetism, fluorescence *etc.*), but also into the nanoparticle–ligand interaction and binding situation. Due to the tremendous scientific effort since the groundbreaking publications of Brust *et al.* about ten years ago,[1] thiolate stabilized gold nanoparticles (AuNPs) meanwhile have become the best understood particle–ligand system so far. Because of the chemical stability of the core they are also the most promising candidate for future applications (*e.g.* in magnetic core–gold shell particles). The Au–S bond is generally believed to be one of the tightest links for gold surface functionalization which is undoubtedly true in terms of thermodynamic stability. On the other hand a reliable functionalization also has to provide kinetic stability against ligand exchange. Especially in a biological environment where SH-groups are present, thiolate–thiol exchange has to be prevented.

$$RS@AuNP + R'SH \rightarrow R'S@AuNP + RSH \qquad (1)$$

Detailed studies of the exchange reaction (1) were performed by the group of R. W. Murray during the last decade. Murray found that for alkanethiolate-covered AuNPs co-dissolved with ω-functionalized thiols the ligand exchange can be proven even after a short reaction time. Different factors having influence on the exchange rate are: 1. the chain lengths of particle bound thiolate ligands and incoming thiols,[2] 2. the position where the exchange

takes place[3] (corners, edges, faces), 3. the size[4] and 4. charge[5] of the particles.

Different efforts have been made to improve the exchange stability of thiolate ligands on AuNPs.[6] Resorcarenes for instance were found to provide high stability against ligand exchange, but the size of the headgroup leads to a lower ligand density on the AuNP surface. This kind of ligand therefore seems to be best suitable for bigger particles with a lower surface curvature.[7] For smaller particles with a high mobility of the outer part of the alkyl chains even when they are closed packed at the nanoparticle surface a high ligand density is preferable. In theoretical models of steric stabilization the ligand density is directly correlated with the repulsive potential (de Gennes)[8] and the brush thickness (Alexander).[9] The brush thickness can be found as half the interparticle distance in dense packed nanoparticle arrays.

For reliable binding to nanoparticles, a chelating long-chain organothiol allowing at the same time colloidal (steric) stabilization by a dense surface coverage should be the ligand of choice.
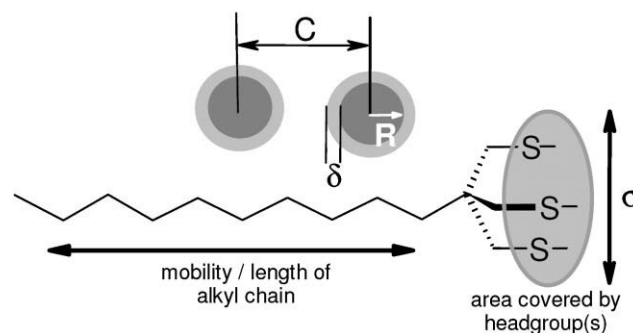

Fig. 1   Ligand geometry and de Gennes parameters of **1**.

We have synthesized the trithiol 1,1,1-tris(mercaptomethyl)undecane[10] **1** as a model to investigate the particle stabilization and exchange properties of a tripodal organothiolate. In Fig. 1, the structure of surface-bound **1** is given together with parameters used in the de Gennes expression[8] for particle stabilization (σ, δ, R, C). The difference between **1** and the commonly used dodecanethiol **2** is given by only two additional thiomethylene "legs", which allows a comparison of the steric stabilization of these two types of ligand systems. In an independent work, Park *et al.* very recently have investigated trithiols such as **1** as components of self-assembled monolayers (SAMs) on gold surfaces; they have described a brush thickness (ellipsometry) and alkyl chain mobility (IR) similar to monodentate thiolates and a remarkably enhanced stability against desorption. The occupied surface of a trithiolate ligand was estimated from XPS-intensities to be about 30 Å².[11]

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We performed monolayer compression experiments with a Langmuir balance to support this value. For **1** on a subphase containing $CdCl_2$ (10 mM) we found an area per molecule of 25–27 $Å^2$. This is comparable with the area occupied by simple surfactants like stearic acid (20 Å).[12] It is yet significantly higher than the area found in the solid state structure of molecular trithiolate complexes. The triangle formed by the three sulfur atoms in $Ir_3(CH_3C(CH_2S)_3)(CO)_6$ covers an area of 12.3 $Å^2$.[13]

For the evaluation of **1** on gold nanoparticles we used two different systems: first, bigger particles with a very narrow size distribution in order to obtain closed packed nanoparticle arrays (AuNP), and second, smaller particles with a higher solubility for precipitation experiments (AuNP′). In both cases **1** was introduced by ligand exchange due to the poor monodispersity of AuNPs prepared in the presence of **1** and for better comparability of **1**@AuNP′ and **2**@AuNP′ (same core size distribution).

For a first evaluation of the nanoparticle stabilization ability of **1** we used with *tetra*-octylammoniumbromide (TOAB)-stabilized AuNPs (Ø 5.5 nm) prepared by the micellar method.[14] The TOAB-stabilized particles were refluxed in toluene with an excess of **1** for 1 h, then precipitated, thoroughly washed (EtOH) and redispersed in toluene to yield a red solution. A TEM image of a sample prepared by dropping 2 μL of the gold nanoparticle (**1**@AuNP) solution onto a TEM grid is given in Fig. 2. The image shows an assembly of particles with regular surface-to-surface distances (2δ in Fig. 1) of 1.5 to 1.8 nm and with a particle radius (R in Fig. 1) of about 2.7 nm. This arrangement is proof of the formation of a dense monolayer of **1** protecting the particles against agglomeration. The elemental composition of this sample determined by EDX (spot size 125 nm on a particle assembly) is shown in the inset of Fig. 3. Beside other elements which can be assigned to the substrate, gold and sulfur can be found in an atomic ratio of x = Au/S = 5.8.

Assuming spherical particles having the bulk density of gold one can estimate the area per tripod-ligand on the particle surface with the term 0.15255 x/r [nm]. The area calculated for the AuNPs described above is ${\sim}30$ $Å^2$ which is in good agreement with the value found in the Langmuir experiment (25–27 $Å^2$).

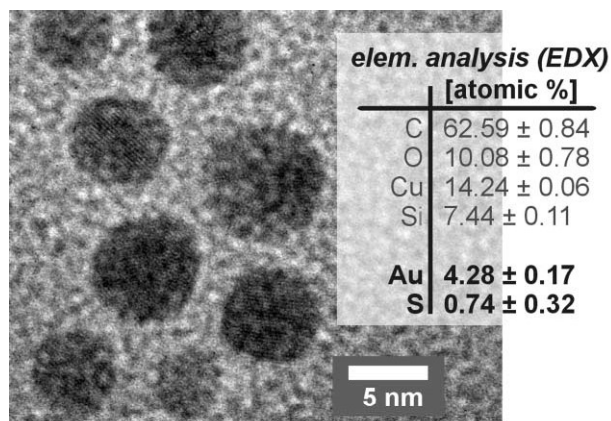| elem. analysis (EDX)	
	[atomic %]
C	62.59 ± 0.84
O	10.08 ± 0.78
Cu	14.24 ± 0.06
Si	7.44 ± 0.11
Au	**4.28 ± 0.17**
S	**0.74 ± 0.32**

Fig. 2 TEM image of trithiolate functionalized particles (**1**@AuNP).

High packing density and sufficient brush thickness are features affecting the steric repulsion and therewith the colloidal stability of ligand protected particles.[8] As demonstrated both objects are accomplished by 1,1,1-tris(mercaptomethyl)alkanes.

As a result of the chelate effect we expect an enhanced exchange stability of **1** against concurrent thiols. For ligand exchange experiments (see Fig. 3) we used smaller gold nanoparticles with a higher solubility prepared in the presence of dodecanethiol (**2**) by a modification of the synthesis developed by Brust[1] (AuNP′, Ø 3.4 ± 0.4 nm). After synthesis, the dodecanethiolate stabilized particles (**2**@AuNP′) were isolated and dissolved in dichloromethane. The addition of 11-mercaptoundecanoic acid (MUNDA) to this particle solution led to the precipitation of a red sediment within a few hours. This observation indicates an easy ligand exchange and a coverage of the particles with polar end-groups (COOH) causing precipitation. For the preparation of particles stabilized with the trithiol **1** (**1**@AuNP′), an excess of **1** was added to a solution of **2**@AuNP′ in CH_2Cl_2 and the resulting solution was stirred at rt for 30 min. The particles were precipitated and dissolved in CH_2Cl_2 + **1** several times (to complete the ligand exchange) and at last dissolved in pure CH_2Cl_2 resulting in **1**@AuNP′. The presence of exchanged **2** in the supernatants is indicated by the characteristic ^{1}H-NMR signal of the α-protons at 2.47 ppm. After addition of MUNDA to the trithiolate-stabilized particles **1**@AuNP′ no precipitation and thus no ligand exchange can be observed.
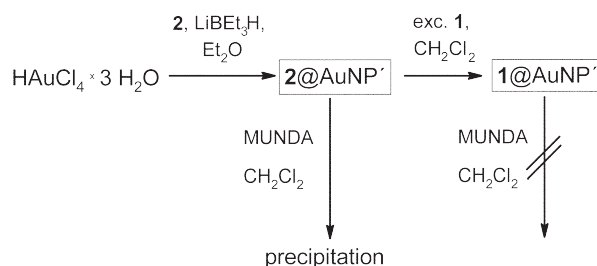

Fig. 3 Ligand exchange experiments with AuNPs (MUNDA = 11-mercaptoundecanoic acid).

A more detailed investigation of the ligand exchange process is possible, if the decay of the plasmon band is monitored during (exchange induced) precipitation.[15] This method can be seen as a time-saving alternative for NMR experiments which require a work up procedure of the solution for every datapoint. Our approach was the *in situ* recording of absorption–time curves after mixing defined molar ratios of particle-attached thiolates and MUNDA in dichloromethane in a quartz cuvette. The concentration of thiolate@AuNP′ in both solutions was calibrated by integrating the respective ligand terminating methyl group ^{1}H-NMR signal compared to the signal of an internal standard of known concentration (TMS). The absorption of the solution was measured at 535 nm with a spectral resolution of 4 nm to allow a slight shift of the plasmon band during the experiment. The total AuNP concentration was adjusted to give a starting absorption of about 1. In case of **2**@AuNP′ a characteristic drop of the absorption can be seen for different concentrations which is in accordance with the precipitation described above. The resulting curves can be fitted with a first order exponential decrease, although in some cases a linear function seems to be superimposed. With a function combining an exponential and a linear part all curves can reasonably be fitted. We believe that the exponential part is due to the ligand exchange and the linear part is due to the

sedimentation and removal of the particles from the observed volume. However this model is still a crude simplification of the real process. The first order constants extracted from the fitted A–t curves are in the range of 10^{-4} s^{-1} and show a slight increase with higher concentrations of the concurrent thiol (MUNDA). This is consistent with the results of Murray obtained for the reaction of hexanethiolate stabilized gold nanoparticles with ω-mercapto-hexanol.[5] As expected from the qualitative observation described above no significant decrease can be found in A–t curves of **1@AuNP′** + MUNDA. In Fig. 4 A–t curves are plotted for both particle types. The initial stoichiometry of MUNDA and particle bound thiolate functions is 1 : 1 in both cases. For **2@AuNP′** the precipitation leads to the characteristic negative slope ($k_{exp} = 1.4 \times 10^{-4}$ s^{-1}). The curve for **1@AuNP′** only shows a small increase caused by solvent evaporation during the experiment.
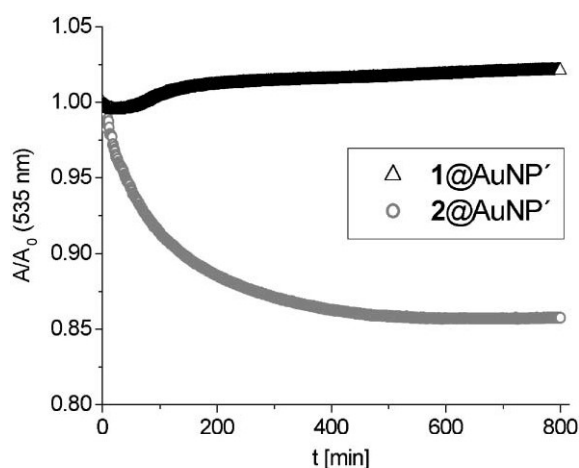

Fig. 4 Typical A–t curve demonstrating the ligand exchange on AuNPs (stoichiometry: RSH/R′S@AuNP′ = 1).

A further functionalization of reliably stabilized nanoparticles can be performed with the help of the recently published[10] ω-unsaturated trithiol 1,1,1-tris(mercaptomethyl)dec-9-ene (**3**). Gold nanoparticles carrying this ligand (**3@AuNP′**) were prepared by the same method as described for **2@AuNP′**.[16] In a first experiment, we have introduced a functional unit by photochemical thiol addition to the peripheral double bond. Thus, UV-irradiation of a CH$_2$Cl$_2$ solution containing **3@AuNP′** and MUNDA led to the formation of the addition product **4@AuNP′** (see Fig. 5) in the form of a red precipitate, which is soluble in dilute aqueous ammonia due to the deprotonation of the peripheral COOH group allowing charge stabilization. An IR absorption at 720 cm^{-1} could be assigned to the thioether group in **4@AuNP′**. The assignment is based on the comparison with the absorption of the thioether group in dioctyl sulfide (721 cm^{-1}).

As a consequence of the chelate effect, an exchange of thiol groups during the reaction shown in Fig. 5 was not observed. Similarly the irradiation of **1@AuNP′** under the same conditions did not produce a water-soluble precipitate.
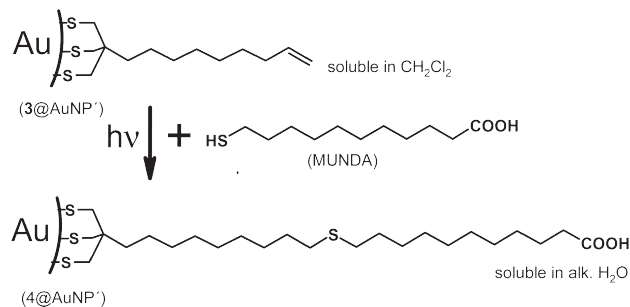

Fig. 5 Functionalization of **3@AuNP′** by reaction with MUNDA.

It can be summarized that 1,1,1-tris(mercaptomethyl)alkanes are novel tripod ligands for the preparation not only of self-assembled monolayers (SAMs)[11] but also for the synthesis of stable nanoparticles. A strong bonding to the particle surface can be ascribed to the chelate effect and to the space saving geometry of the thiolate groups. No thiolate exchange is observed after addition of a concurrent monothiol. 1,1,1-Tris(mercaptomethyl)alkanes with a terminal double bond can be used for the functionalization of nanoparticles using standard synthetic methods. Although our work so far has concentrated on gold nanoparticles, the strategy should be applicable also in the context of other core materials commonly stabilized with thiolate ligands. This method is of special importance for the reliable bio-functionalization of particles, which currently is a fast growing field.[17]

Notes and references

1 M. Brust, M. Walker, D. Bethell, D. J. Shiffrin and R. Whyman, *J. Chem. Soc., Chem. Commun.*, 1994, 801; M. Brust, J. Fink, D. Bethell, D. J. Shiffrin and C. Kiely, *J. Chem. Soc., Chem. Commun.*, 1995, 1655.
2 R. S. Ingram, M. J. Hostetler and R. W. Murray, *J. Am. Chem. Soc.*, 1997, **119**, 9175.
3 M. J. Hostetler, A. C. Templeton and R. W. Murray, *Langmuir*, 1999, **15**, 3782.
4 R. Guo, Y. Song, G. Wang and R. W. Murray, *J. Am. Chem. Soc.*, 2005, **127**, 2752.
5 Y. Song and R. W. Murray, *J. Am. Chem. Soc.*, 2002, **124**, 7096.
6 B. Garcia, M. Salome, L. Lemelle, J.-L. Bridot, P. Gillet, P. Perriat, S. Roux and O. Tillment, *Chem. Commun.*, 2005, 369; B. Kim, R. Balasubramanian, W. Perez-Segarra, A. Wei, B. Decker and J. Mattay, *Supramol. Chem.*, 2005, **17**, 1–2, 173–180.
7 A. Wei, *Chem. Commun.*, 2006, 1581.
8 $E_{pot} \approx 100R\delta^2/((C - 2R) \pi\delta^3)kT\cdot\exp[-\pi(C - 2R)/\delta]$: B. A. Korgel, S. Fullam, S. Connolly and D. Fitzmaurice, *J. Phys. Chem. B*, 1998, **102**, 8379; P. G. de Gennes, *Adv. Colloid Interface Sci.*, 1987, **27**, 189.
9 S. Alexander, *J. Phys.*, 1977, **38**, 983.
10 K. Wojczykowski and P. Jutzi, *Synlett*, 2006, 1, 39.
11 J.-S. Park, A. N. Vo, D. Barriet, Y.-S. Shon and T. R. Lee, *Langmuir*, 2005, **21**, 2902.
12 H.-D. Dörfler, *Grenzflächen- und Kolloidchemie*, VCH, Weinheim, 1994, p. 69.
13 A. Maisonnat, J. Devillers and R. Poilblanc, *Inorg. Chem.*, 1987, **26**, 1502.
14 J. Fink, C. J. Kiely, D. Bethell and D. J. Shiffrin, *Chem. Mater.*, 1998, **10**, 922.
15 R. Balasubramanian, B. Kim, S. L. Tripp, X. Wang, M. Liebermann and A. Wei, *Langmuir*, 2002, **18**, 9, 3676.
16 **3@AuNP**: <*D*> 4.3 = nm.
17 H. Gu, K. Xu, C. Xu and B. Xu, *Chem. Commun.*, 2006, 941.