Vibrational circular dichroism of *N*-acetyl-L-cysteine protected gold nanoparticles†

Cyrille Gautier and Thomas Bürgi*

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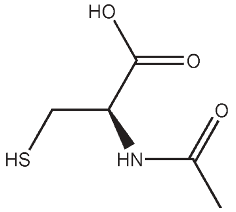
Vibrational circular dichroism is used to determine the conformation of a thiol adsorbed on gold nanoparticles.

Monolayer protected metal nanoparticles are of considerable interest due to their potential application in various fields such as bio-sensing, catalysis, electronics and nanotechnology.[1] Whereas the physical properties of monolayer protected nanoparticles (MPNs) are largely associated with the metal core, their chemical behaviour such as solubility, molecular recognition and organization, is determined by the protection layer. The engineering of the latter is currently making tremendous progress.[2] The conformation of the molecules adsorbed on the metal particles directly affects the chemical properties. Structure determination would therefore greatly help the rational design of functionalized particles.

Vibrational circular dichroism (VCD) spectroscopy, *i.e.* the differential absorption of left and right circular polarized infrared light, yields detailed information on the conformation of a chiral molecule in solution.[3] VCD is more sensitive towards conformation than infrared (IR) spectroscopy and its power for structure determination of dissolved molecules, by the comparison between experimental and theoretical spectra, has impressively been demonstrated in the past.[4–7]

In this contribution we show that very small (<2 nm) gold nanoparticles chirally modified with *N*-acetyl-L-cysteine (Scheme 1) exhibit VCD activity associated with the molecules in the protection layer. Comparison with calculated VCD spectra of *N*-acetyl-L-cysteine adsorbed on small gold clusters allows getting rather detailed structural information. Whereas optical activity in the UV-vis of MPNs has been reported before,[8] to the best of our knowledge this is the first report on the VCD activity associated with MPNs.



Scheme 1 Structure of *N*-acetyl-L-cysteine.

The MPNs were prepared following a previous report.[9] 400 mg of tetrachloroauric acid (1.01 mmol) and 663 mg *N*-acetyl-L-cysteine (4.06 mol) were dissolved in 200 ml of 6 : 1 methanol : acetic acid, giving a red solution, which rapidly turned into a cloudy white suspension. This indicates the formation of a Au(I)–*N*-acetyl-L-cysteine polymer.[10] After 15 min, the polymer was reduced by slow addition of a freshly prepared aqueous $NaBH_4$ solution (70 ml, 2.13 mol l^{-1}) under vigorous stirring. After 90 min of additional stirring, the resulting solution was filtered using 0.2 μm PTFE membranes (Millipore) to remove precipitates and subsequently evaporated under vacuum to near dryness. The nanoparticles were purified in two steps. The first one consisted of a series of precipitations with ethanol and filtration using 0.2 μm PTFE membranes. The removal of the remaining unreacted thiol or disulfide was finally completed by dialysis (Spectra/Por CE, molecular weight cut-off MWCO = 3 500). Particles were dissolved in 30 ml water and loaded into a membrane, which was then placed in a 2 l beaker of water and slowly stirred. The water was changed every 10 h over the course of 96 h. The black solution was evaporated under vacuum at $T \leqslant 40$ °C to give a black powder.

Transmission electron microscopy (TEM) revealed gold particles with a maximum in the core size distribution below 2 nm (see electronic supplementary information†). This is in good agreement with the UV-vis spectrum of the sample, which showed almost no surface plasmon resonance, thus revealing that the gold particles have core diameters of 2 nm or less.[11]

The ^{1}H and ^{13}C NMR spectra of the sample (see electronic supplementary information†) are consistent with *N*-acetyl-L-cysteine adsorbed on the gold particles. Compared to the free molecule the resonances are significantly broadened. The absence of sharp resonances showed that the sample contained no free *N*-acetyl-L-cysteine molecules.

Fig. 1 shows the experimental infrared and VCD spectra of the *N*-acetyl-L-cysteine protected gold nanoparticles. In D_2O some of the acid groups are not deprotonated. NaOD was therefore added in order to achieve complete deprotonation. Based on titration experiments the carboxylate vibrations $\nu_s(COO^-)$ and $\nu_{as}(COO^-)$ can easily be assigned to bands at 1387 and 1595 cm^{-1}. The former signal contains also the symmetric CH_3 deformation mode $\delta_s(CH_3)$, since a weak band below 1400 cm^{-1} is also observed in the fully protonated state. The amide I vibration is located at 1627 cm^{-1}. The rather broad feature around 1480 cm^{-1} is assigned to the amide II mode of the deuterated (N–D) molecules.[12] The band around 1425 cm^{-1} can be assigned to the $\delta_{as}(CH_3)$ mode. The CH_2 scissoring mode also contributes to this band. This assignment is supported by the calculations (see below) and

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Université de Neuchâtel, Institut de Chimie, Rue Emile-Argand 11, 2007-Neuchâtel, Switzerland. E-mail: thomas.burgi@unine.ch; Fax: +41 32 718 24 12; Tel: +41 32 718 25 11

† Electronic supplementary information (ESI) available: Experimental details, TEM, UV-vis, NMR, calculated conformers of Au_{19} cluster, calculated IR spectra, full ref. 16 and ref. 17. See DOI: 10.1039/b509346e

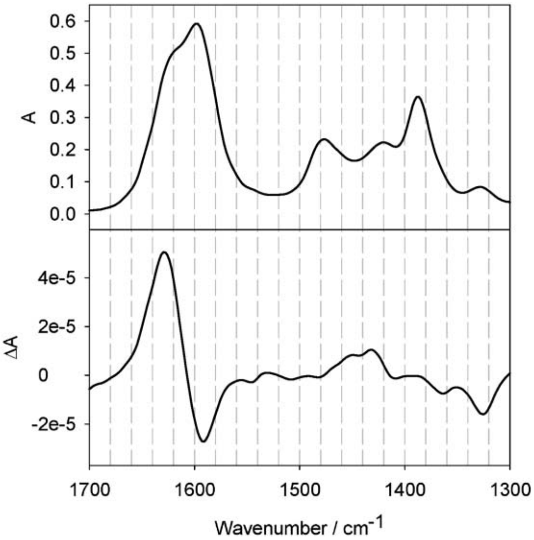

Fig. 1 Infrared (top) and VCD (bottom) spectra of *N*-acetyl-L-cysteine protected gold nanoparticles in D_2O. NaOD was added to deprotonate all acid groups. The solution was made from 8 mg sample in 70 µl solvent.

follows the assignment given by Pradier and coworkers for cysteine adsorbed on Cu(110).[13] Finally, the weaker band at around 1330 cm^{-1} is due to a CH bending mode.

In order to extract structural information, the experimental VCD spectra have to be compared to calculated ones for the relevant conformers. The *N*-acetyl-L-cysteine protected nanoparticles investigated here contain 20–200 gold atoms (1–2 nm core diameters) and up to several tens of adsorbed *N*-acetyl-L-cysteine molecules. The entire particle is too large to be calculated at the required accuracy and therefore models have to be used. Such an approximation is justified since molecular vibrations are a local property. For example, the vibrational spectrum of molecules adsorbed on a metal surface can be reproduced very well by calculations that consider only one single molecule adsorbed on a small cluster of a few atoms.[14,15]

N-Acetyl-L-cysteine has several pertinent conformational degrees of freedom, namely the rotations around the three bonds comprising the chiral carbon atom (one C–N and two C–C bonds, Scheme 1). Potential energy minima are largely determined by the hydrogen bond between the amide N–H and the carboxylate group. The part comprising the amide and methyl group on the other hand is rather rigid.

To explore the potential energy surface for *N*-acetyl-L-cysteine adsorption on gold, cluster calculations were first performed using ADF.[16] It should be noted here that upon adsorption a thiolate is formed and therefore the corresponding thiolate of *N*-acetyl-L-cysteine was considered in the calculations. A gold 19 cluster served as a model. The positions of the gold atoms were fixed at their bulk interatomic distance. The adsorption is primarily determined by the strong Au–S bond. We found that an additional interaction *via* the carboxylate leads to considerable stabilization. (Some stable adsorption geometries are given in the supplementary information.†) It should be mentioned here that the relative stability of the different conformers is likely to be affected by intermolecular interactions between adjacent molecules, which are neglected in the calculations. However, the relative stability of a conformer is not used as the primary argument for structure determination. It is rather the comparison between calculated and experimental VCD spectra that yields this information and the vibrational properties are much less affected by weak intermolecular interactions.

The size of the cluster was then further reduced in order to calculate VCD spectra of adsorbed *N*-acetyl-L-cysteine using Gaussian03.[17] We first considered the four gold atoms of the larger Au_{19} cluster that directly interact with the molecule. The structure of the adsorbed *N*-acetyl-L-cysteine was then re-optimized, keeping the positions of the gold atoms in the Au_4 cluster fixed. Structure a′ in Fig. 2 is the result of such a calculation. Fig. 3 shows the calculated VCD spectrum (trace a′) for this structure. (The corresponding IR spectrum is given in the supplementary information.†)

For the calculations of structure a′ in Fig. 2 the positions of the gold atoms were fixed as described above. Complete relaxation of all degrees of freedom, including the Au atoms, led to structure a, where the four gold atoms adopt a tetrahedron. The conformation of the adsorbed *N*-acetyl-L-cysteine on the other hand hardly changed with respect to structure a′. The VCD spectra of structures a′ and a are very similar, indicating that the nature of the gold cluster has only a minor influence on the vibrations located within the molecule. The intensity of $\nu_s(COO^-)$ and the C–H bending mode decreased (bands with labels 2 and 1 in Fig. 3) and the $\nu_{as}(COO^-)$ mode shifted in frequency when going from the planar to the tetrahedral Au_4 cluster.

Fig. 2 shows other conformers that were calculated. All of these were found to be less stable than conformer a. Conformers b and d also interact *via* the carboxylate group with the Au_4 cluster, whereas conformer c interacts *via* the amide group. The difference between the most stable conformer a and conformer d is at the level of the CH_2 and COO^- groups. Fig. 3 shows that the VCD spectra strongly depend on the conformation of the adsorbed *N*-acetyl-L-cysteine. This is most evident from the signals associated with the amide I and $\nu_{as}(COO^-)$ vibrations. Both bands are negative for conformations b and c, whereas both are

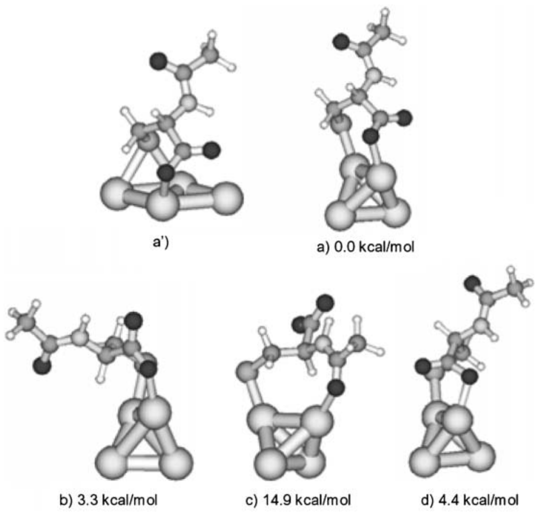

Fig. 2 Calculated conformers of deprotonated *N*-acetyl-L-cysteine on a Au_4 cluster. The structures were optimized using Gaussian03.[17] For structure a′ the Au_4 cluster was fixed. For the other structures all degrees of freedom were relaxed during optimization. The numbers indicate the relative stability with respect to the most stable conformation, a.

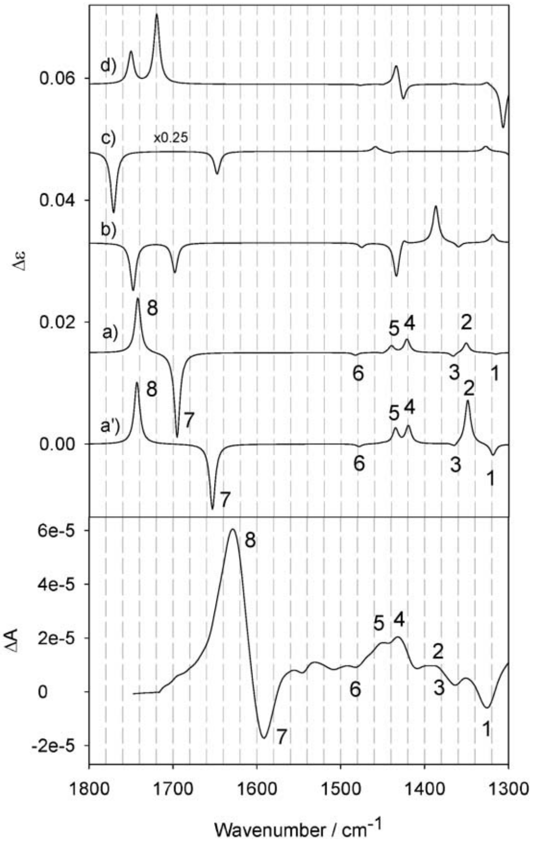

Fig. 3 VCD spectra for the structures shown in Fig. 2 (top) compared to the experimental spectrum (bottom). Labels indicate corresponding bands.

positive for conformation d. Only conformer a (and a′) have the correct sign for both bands. However, the rest of the spectrum also gives the best fit between calculated and experimental spectra for conformation a (a′), particularly bands 4 and 5 and also the C–H bending mode (band 1), which is clearly negative in the experimental spectrum.

The results presented above show that chiral molecules adsorbed on small gold particles exhibit VCD activity. The experimental and calculated spectra for the most stable conformer of the adsorbed molecule are in reasonable agreement, indicating that the applied computational strategy, despite the inherent approximations, is reliable. The calculations indicate that the VCD spectrum is more sensitive to the conformation of the molecule than towards the structure of the metal particle onto which the molecule is attached. Still, the (unknown) local structure of the adsorption site represents an uncertainty for the calculation of VCD spectra of adsorbed molecules, which may explain some differences between experimental and calculated spectra.

The proposed structure (Fig. 2a, a′) strongly resembles the one determined for cysteine adsorbed on Cu surfaces by reflection absorption infrared spectroscopy,[18] in particular the part comprising the adsorbed thiol and carboxylate groups. In cysteine the amine group points away from the surface as does the amide group in *N*-acetyl-L-cysteine. It should also be pointed out that in this adsorption geometry the molecule occupies only a little space, which allows high coverage on the metal particle surface. The latter property contributes to the high stability of the particles by preventing the metal cores from agglomeration.

MPNs can be viewed as the nanometre-sized analogues of self-assembled monolayers (SAMs) on extended metal surfaces.[19] An increasingly important class of metal surfaces are those modified with a chiral molecule,[20–21] which have for example been used for heterogeneous enantioselective catalysis[22] and chiral discrimination.[23–24] The discrimination between and separation of enantiomers or the selective production of one enantiomer is of great importance, as chirality is a fundamental aspect of molecular biology. The structure of the adsorbed molecules plays a fundamental role in these processes. Our results indicate that VCD spectroscopy may greatly help in elucidating the structure of chiral molecules adsorbed on metal particles.

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