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COMMUNICATION

# Synthesis and characterization of mixed ligand chiral nanoclusters

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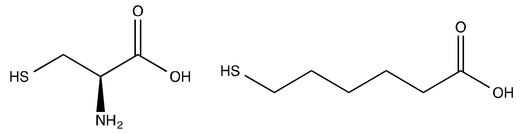
**Chiral mixed ligand silver nanoclusters were synthesized in the presence of a chiral and an achiral ligand. The ratio of the ligands was changed to track the formation of these clusters. While the chiral ligand lead to mostly to the forming of nanoparticles, the presence of the achiral ligand drastically increased the yield of nanoclusters with enhanced chiral properties.**

Clusters of metal atoms have attracted attention since they provide a size scale that bridges the properties of the atomic and nanoscale. In this size scale (2 nm and below),[1] unique properties such as intense absorption peaks covering visible and near IR spectra,[2–4] tunable florescence,[5–8] and discreet electronic transitions[9–11] can be observed. These properties combined with their small size, make nanoclusters sought after materials for possible applications in catalysis,[12–15] sensing,[16,17] and light harvesting[2,18,19]. In addition, cluster/biomolecule complexes were used to detect phenol compounds or drugs[20,21] while cluster doped nanoparticles/nanowires were utilized to increase the catalytic activity of nanostructures[8,22–25].

The introduction of chiral properties to these clusters could extend their applications in chiroptical devices,[26–28] enantioselective catalysis,[29–31] as well as in new sensing methods[20,32,33]. To impart chirality, usually a chiral ligand, such as D-L-penicillamine,[34] D-L glutathione[33,35] or N-acetyl-L-cysteine,[36] is used to stabilize the cluster of atoms. While several biomolecules provide chiroptical activity in near UV, these metal/chiral ligand complexes are active in the UV-Visible (UV-Vis) range due to discrete energy bands of the metal part[37–39]. Hybrid complexes of metals and chiral ligands can facilitate the design of biosensors since these complexes have amplified CD signals compared to biomolecules[35]. Kitaev and Cathcart also reported the generation of mixed ligand chiral silver clusters and showed that the presence of two chiral ligands enhanced the chiroptical behavior of these clusters.[40]

Here, we show the synthesis and characterization of water-soluble chiral silver nanoclusters that are stabilized with a mixed ligand system: the chiral L-cysteine (L-cys) and the achiral mercaptohexanoic acid (MHA) (Scheme 1). In the reaction conditions that were tested, the use of MHA was critical for the formation of chiral nanoclusters compared to homoligand L-cys-stabilized silver nanoparticles. A nanocluster of ~10 kDa was consistently encountered even at different starting ligand ratios suggesting the stability of the complex of metals atoms with the ligands. To our knowledge, it is the first class of nanoclusters in which the existence of non-chiral ligand prompted the chiral behavior.



**Scheme 1**Chemical structures of L-cys and MHA

Mixed ligand silver nanoclusters were synthesized by reducing silver nitrate in methanol and water mixture at room temperature (RT). To determine the matrix of conditions that produce clusters, we systematically changed i) ligand and ii)

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silver to thiol ratio. In the UV-Vis spectrum, the peaks that are approximately around 385 and 550 nm indicate the formation of clusters similar to Ag32 stabilized with glutathione[41]. The peak below 400 nm is the characteristic of electronic interaction of metal core and ligands[42] and the peak at 550 nm is attributed to the metal core and its discrete energy levels[41]. At a constant silver to thiol ratio (1:1), ligand ratios of 1:1, 1:2, and 1:3 L-cys:MHA provided almost overlapping UV-Vis spectra (Fig. 1); this overlap implied the formation of very similar structureswith different yields when different amounts of ligands were present in the reaction mixture. However, the use of solely L-cys lead to the formation of silver nanoparticles that revealed a characteristic peak at 440 nm that might be due to surface plasmon resonance of silver.

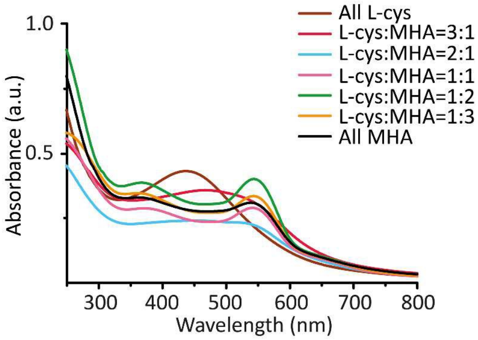

**Fig.1** UV-Vis spectra of the structures with different ligand ratios

To determine the different classes of clusters that are possibly formed during the synthesis, the reaction products of 7 different ligand ratios were separated via PAGE (Fig. 2a). To examine the bands further, we chose one of the synthesis with high yield (1:1 ligand ratio) and extracted 6 different bands from the gel. UV-Vis spectroscopy revealed that band 4 contains nanoclusters that were presented in UV-Vis of as-synthesized nanoclusters (Fig. 2b).

Band 4 of other reactions with 2:1, 1:2, 1:3 and pure MHA also displayed similar UV-Vis spectra. For each synthesis we also monitored the chirality of this dominant band via CD spectroscopy. The band 4 in each sample produced similar CD spectra underscoring the formation of a dominant cluster at mixtures with different ligand ratios (Fig. 3a, 3b). To investigate this similarity, we carried out Nuclear Magnetic Resonance Spectroscopy (NMR) on band 4 of reactions with starting ligand ratios of 1:1, 1:2, and 1:3. Relative ratios of the ligands on the etched clusters were calculated by comparing the spectrum of etched pure ligands. The results showed the ratio of L-cys on these clusters is approximately 10% underlying the importance of MHA in cluster synthesis (Fig. S3).

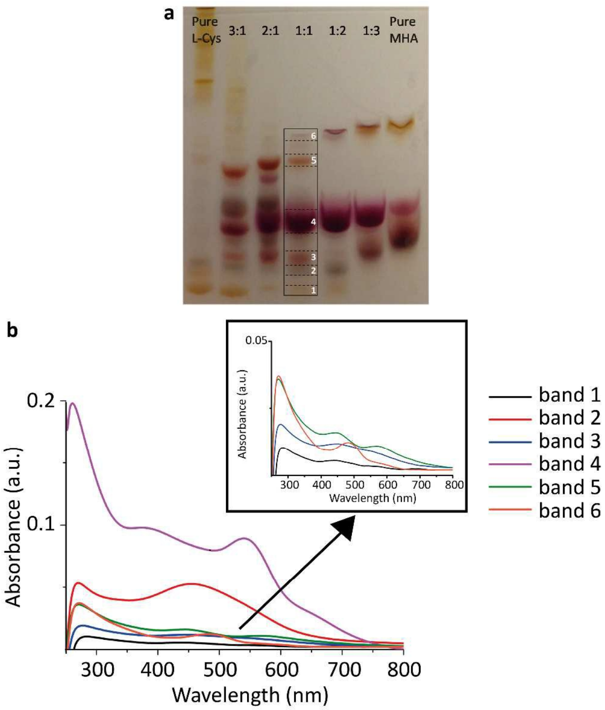

**Fig.2 (a)** PAGE of the as-synthesized structures with different ligand ratios, **(b)** UV-Vis spectra of PAGE fractions of the sample with L-cys: MHA ratio of 1:1

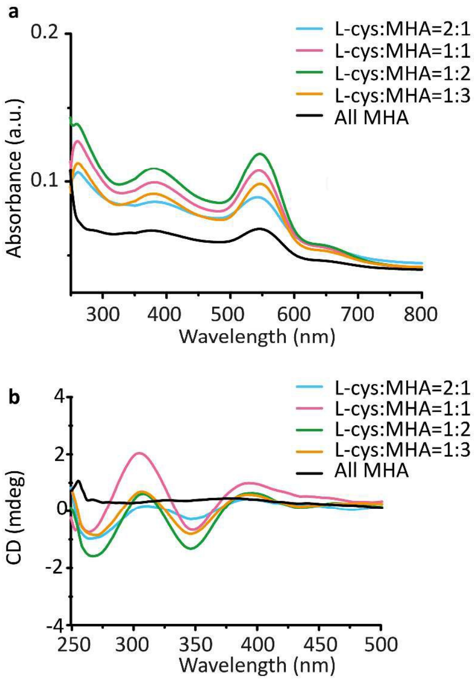

**Fig. 3(a)** UV-Vis spectra of the band 4from the PAGE of the samples with different L-cys: MHA ratios, **(b)** CD spectra of the same samples

In addition, when we changed silver to thiol ratio of these clusters at equimolar contributions from L-cys and MHA, wealso observed the formation of clusters at ratios of 1:1, 1:1.25, and 1:1.5; but at the ratio of 1:2 only a small amount of clusters was formed (Fig. S1). The chirality of mixed ligand clusters was further investigated by carrying out the experiments with a molecule of reverse chirality, D-cysteine (D-cys). We again observed the formation of clusters but with reverse chirality (Fig. S2). This result indicates that chirality of these clusters is due to chiral ligand-based formations.

For the characterization of the size of these clusters, we utilized mass spectrometry on band 4. However, we were unable to get a conclusive mass spectrum with ESI and MALDI in aqueous saturated solution of 2, 5 dihydrobenzoic acid and α-cyano 4-hydroxycinnamic acid as a matrix. Using laser desorption ionization (LDI), we found a single broad cluster peak at ~12.5± 3 kDa (Fig. 4S). This result is in agreement with the resemblance of these clusters to glutathione-Ag32 that has a size of 9.27 kDa.

During synthesis, the formation of red/pink nanoclusters starts after an hour and we stop the reaction after 6 hours. If the clusters are left at room temperature (RT) in the reaction mixture, they aggregate irreversibly. To examine the effect of temperature and solvent on the stability of the clusters, we kept the clusters in i) their initial reaction environment (water/methanol solution at a pH of 11), ii) water/methanol solution, and iii) water. We also stored these solutions at −18 °C, 4°C, and RT.

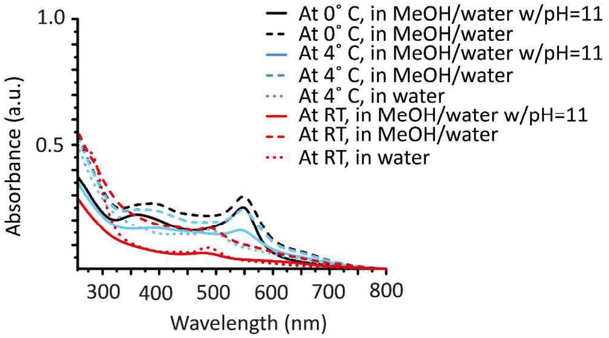

**Fig. 4** UV-Vis spectra of samples with L-cys: MHA ratio of 1:1 that were kept at −18 0°C, 4 °C, and RT in water, water/methanol solution, and initial reaction conditions for 3 weeks.

We observed a color change in the samples that are kept at RT just after 4 days while the others preserved their color. To monitor the long-term stability, we performed UV-Vis spectroscopy after 3 weeks. The absorption peaks of clusters at 550 nm were preserved in the samples that were kept at −18°C and 4°C in methanol/water solution at high pH and in the initial reaction environment (Fig 4).

In conclusion, we synthesized chiral nanoclusters with a binary ligand system. We observed that the formation of nanoclusters is linked to the presence of the achiral ligand, MHA, whereas the chirality results from the presence of both ligands i.e. L-cys and MHA together. Additionally, regardless of ligand ratio, in most of the binary (chiral-achiral) ligand systems we observed the formation of chiral nanoclusters with similar chemistry to 10% L-cys.

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