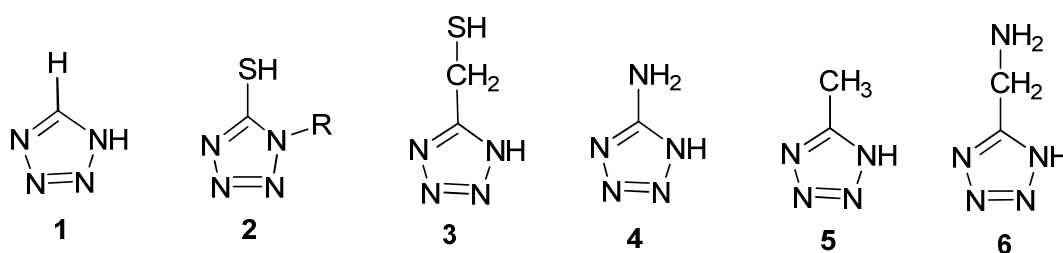


Development of tetrazole-capped nanocrystals for plasmonic sensor applications

Tetrazole (**1**) and its derivatives are an exotic class of organic heterocyclic compounds which contain a five-membered ring of four nitrogen atoms and one carbon atom (Scheme 1). Tetrazoles are not presented in nature and living bodies, however being metabolism-resistant isosteric replacements for carboxylic acids and *cis*-amides they play an important role in biochemistry and pharmaceuticals. The tetrazolyl moiety is presented in the composition of some widely known newest drugs: bactericidal (Kefzol), cardiovascular (Losartan) medicines, and some others. Moreover, tetrazolium salts are used in the MTT assay of the respiratory activity of live cells in cell culture. Owing to the presence of several donor endocyclic nitrogen atoms tetrazole derivatives are attractive as ligands for preparation of metal complexes which are of academic and industrial interest in some hot topics like metal-organic frameworks, light-emitting devices, molecular magnetism, nonlinear optics, and others [1].



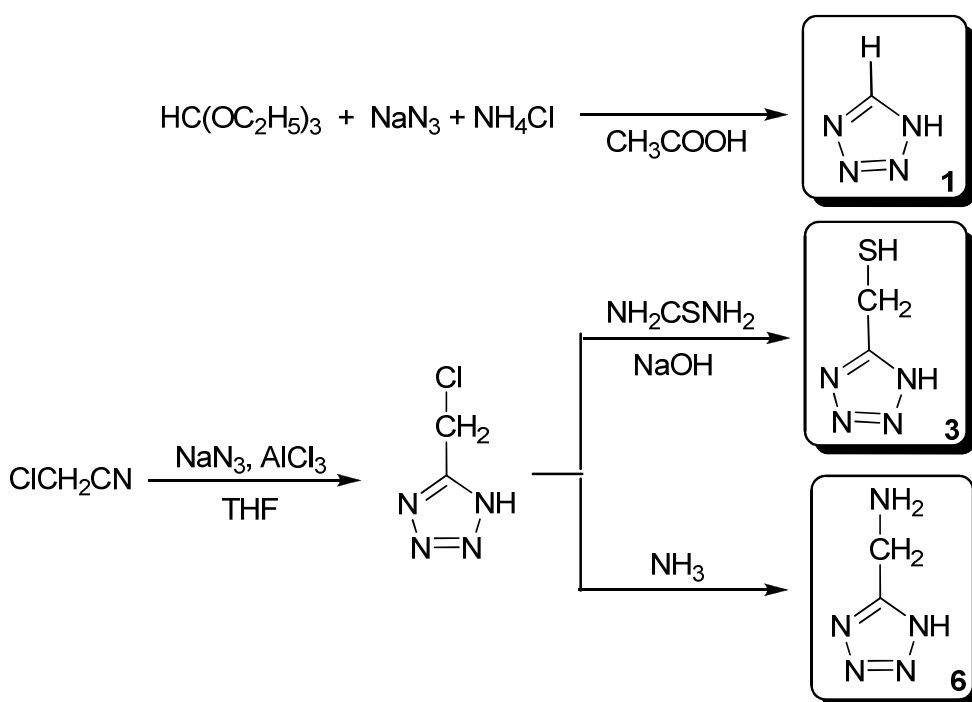
Scheme 1. Structural formulas of tetrazole and its derivatives.

Our recent studies showed perspectives of tetrazoles as capping agents for nanoparticles (NPs) preparation. In particular, we have shown that easily available 1-R-tetrazole-5-thiols (**2**), can be used for chemical synthesis of cadmium sulphide [2] and noble metal (Au, Ag, Pd, Pt) [3] NPs. 5-Mercaptomethyltetrazole (**3**) was found to be a good substitute for thioglycolic acid, which is widely used as a capping agent in the aqueous synthesis of colloidal semiconductor quantum dots. Usage of this ligand allows preparation of high luminescent water soluble semiconductor cadmium telluride NPs possessing the unique ability to reversibly form fine 3D networks (hydrogels) upon addition of metal salts [4]. In such networks built of cadmium telluride quantum dots and gold nanoparticles efficient exciton – plasmon coupling was observed and related effects of plasmon enhanced emission were

investigated [5]. 5-Aminotetrazole (**4**) and 5-methyltetrazole (**5**) were applied for a synthesis of Ag NPs in water [6]. It was found that obtained NPs capped with tetrazoles **4** and **5** tend to agglomerate, which allows controllable *in situ* monitoring of the changes in the optical properties utilizing UV/Vis- and Raman-spectroscopy.

Continuing our earlier synthetic and optical investigations of metal NPs capped with tetrazole derivatives in framework of Research Networking Programm “Plasmon-Bionanosense” we aimed to investigate behavior of parent tetrazole **1** and its functionally substituted derivatives, in particular 5-mercaptomethyltetrazole (**3**) and tetrazolyl analogues of amino acid glycine, 5-aminomethyltetrazole (**6**) as a capping agents for stabilization of metal NPs possessing plasmonic behavior. Moreover, study of optical properties of tetrazole-capped NPs and sensitivity of plasmonic behavior NPs towards the additional metal ions were planned.

The research was done in the group of Prof. Dr. Alexander Eychmüller (Physical Chemistry/Electrochemistry, Dresden University of Technology, Germany). Tetrazole and its derivatives have been synthesized by well-known procedures [4, 7, 8] according to the Scheme 2.



Scheme 2. Synthesis of tetrazole derivatives.

Depend on structure of tetrazole ligand different approaches were investigated in order to prepare tetrazole-capped NPs. In first approach we introduced tetrazoles during nanocrystal synthesis by employing them as stabilizing agents. Alternatively, surface ligand exchange procedure was used.

We found that reduction of silver nitrate with sodium borohydride in the presence of tetrazole **1** in water yields silver NPs. According to data of transmission electron microscopy (TEM) silver NPs capped with tetrazole **1** have spherical shape with the average size varied from 10 to 20 nm. In the UV-Vis spectra of the freshly prepared silver NPs peak was observed near 400 nm. Surface Enhanced Raman Scattering (SERS) spectra of NPs prepared is characterized with strong band at 240 cm^{-1} which is characteristic for the Ag-N stretching-vibration and proves that the tetrazole is bound to the nanoparticle surface. The region $600\text{--}1500\text{ cm}^{-1}$ shows various bands that are mainly originating from different ring vibration modes. It should be noted that solutions of NPs show stability for a week at room temperature. During this time the yellow solution becomes colourless and crystalline product is formed. According to X-ray diffraction study this product was identified as silver tetrazolate $\text{Ag}(\text{HCN}_4)_2$, which is formed by oxidative degradation of silver NPs by air oxygen catalyzed with tetrazole.

Reduction of tetrachloroauric acid with sodium borohydride in water was found to yield very small ($<3\text{ nm}$) gold NPs showing stability for 2 weeks in aqueous solution. In the UV-Vis spectra of the freshly prepared NPs low intensive peak was observed at 540 nm. Under storage of NPs solution the intensity of this peak is decreased and new one is appeared at 660 nm and further it is shifted till 700 nm due to agglomeration of NPs.

In analogous conditions tetrazoles **3** and **6** didn't produce stable metal NPs. Only insoluble precipitates have been obtained under reduction of metal salts with borohydride in presence of above mentioned tetrazoles. However, surface ligand exchange procedure was found to be successful for preparation of silver and gold NPs capped with 5-mercaptomethyltetrazole **6** from corresponding NPs capped with citrate and borohydride anions. Initial citrate-functionalized gold NPs with size $15 \pm 2\text{ nm}$ and borohydride-stabilized silver NPs with size $10 \pm 5\text{ nm}$ were prepared following the procedures published elsewhere [9, 10]. It should be noted that tetrazoles **1** and **6** didn't replace above mentioned capping ligands from the surface of metal NPs.

Prepared silver and gold NPs capped with 5-mercaptomethyltetrazole **6** showed high stability (more than 2 months) in concentrated aqueous solutions ($C_{\text{metal}} \approx 0.025\text{--}0.04\text{ mol/l}$). Obtained NPs showed plasmon bands at 423 and 522 nm, correspondingly. These bands are not shifted under storage. In contrast to NPs capped with tetrazole **1**, Ag-N stretching-vibration band is absent in region of $200\text{--}300\text{ cm}^{-1}$ in the SERS spectra of NPs capped with tetrazole **6**. This indicates that ligand **6** is bound to the nanoparticle surface through sulfur atom, but not through heterocycle.

Taking into account strong coordination ability of tetrazole moiety in relation to different metal ions [11] the behavior of the 5-mercaptopomethyltetrazole-capped NPs towards the additional metal ions was studied. We found that tetrazole-capped NPs are sensitive to alkaline-earth and transition metal ions, like Ca^{2+} , Ba^{2+} , Al^{3+} , Cu^{2+} , Zn^{2+} . Addition of these metal ions leads to agglomeration of NPs accompanying with changes in optical properties. Figure 1 shows the evolution of UV-Vis spectra of gold NPs under action of calcium chloride and bis(ethylenediamine)copper(II) perchlorate.

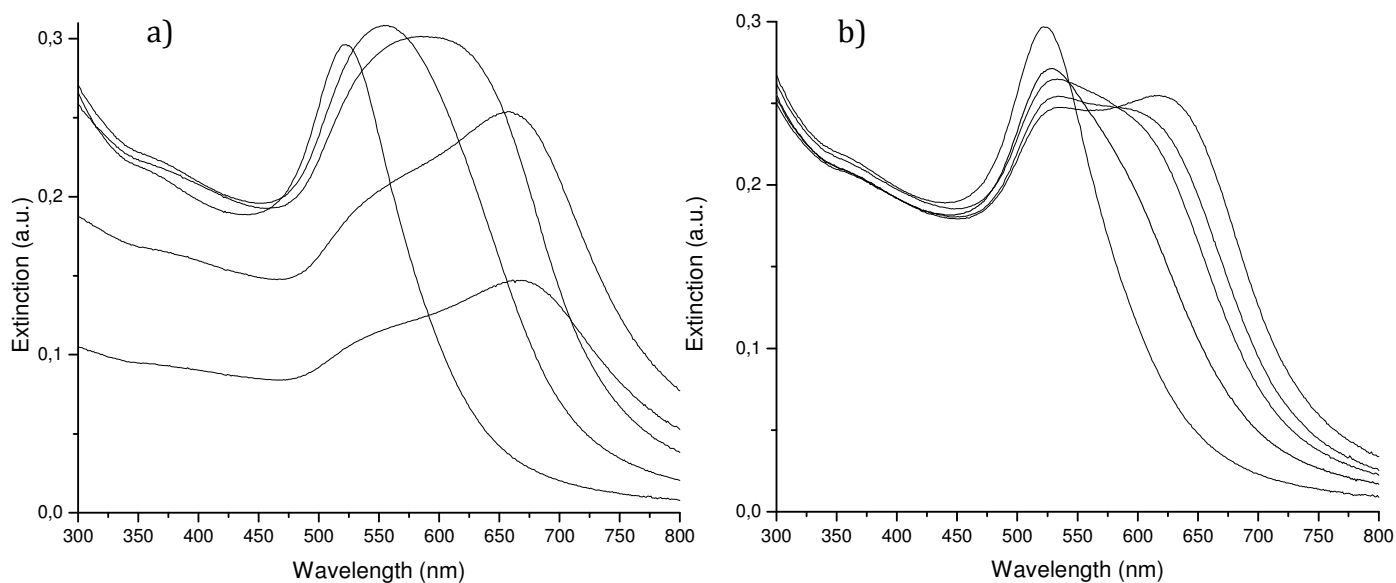
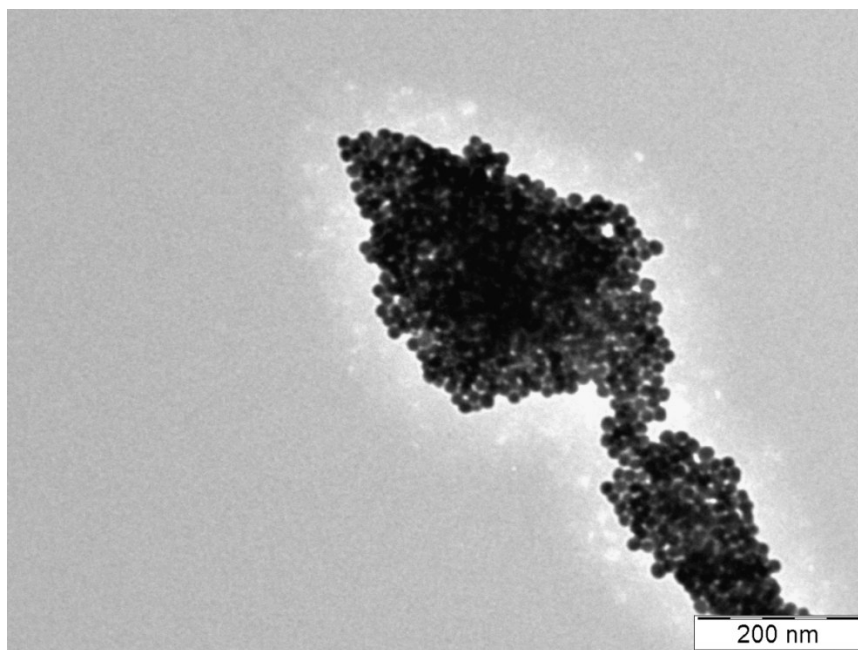


Figure 1. Evolution of UV-Vis spectra of gold NPs capped with tetrazole **3** under action of calcium chloride (a) and bis(ethylenediamine)copper(II) perchlorate (b).

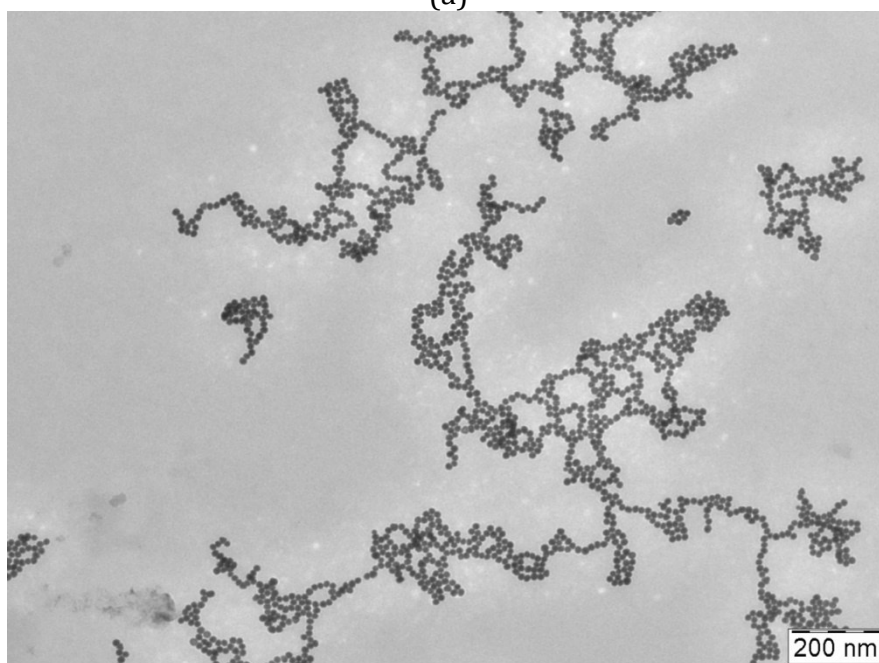
Changes of plasmonic behavior of NPs can be explained by agglomeration of single NPs due to the cross-linking of individual particles by the complexation of tetrazolate units with additional metal cations. Transmission electron microscopy (TEM) studies approved formation of agglomerates (Figure 2). Changes of plasmonic behavior of NPs as well as shape and size of agglomerates formed are strongly depend on nature and concentration of metal ions added. Big discrete aggregates are formed under action of calcium ions whereas chain structures are formed in presence of Cu^{2+} ions fixed with ethylenediamine. Probably, such differences are due to different coordination of metal ions with capping ligand attached to the surface of NPs. Copper ions can bind only two single NPs. At the same time calcium ions have higher coordination numbers (till 6-12) and can bind few NPs. Similar changes of plasmonic behavior were also observed for under action of metal salts on silver NPs capped with tetrazole **6**.

We also found that increasing of concentration of metal ions added leads to the formation of hydrogels. Hydrogels are formed on the bottom of the flask within relatively short times

(from a few seconds up to weeks, depending on the amount of metal salts used). This method offers a facile and highly reproducible interconnection of NPs leading to a multibranched network. The TEM image clearly shows the random orientation of the NPs and their networking in the gel structure under action of zinc acetate on aqueous solution of 5-mercaptopethyltetrazole-capped gold NPs (Figure 3). It should be noted that the technique described does not involve any sophisticated processing like chemical destabilization of the initial colloid or its photochemical treatment as used for preparation of silver and gold gels [12].



(a)



(b)

Figure 2. TEM images of tetrazole-capped gold NPs agglomerated under action of calcium chloride (a) and copper(II)-bis(ethylenediamine) perchlorate (b).

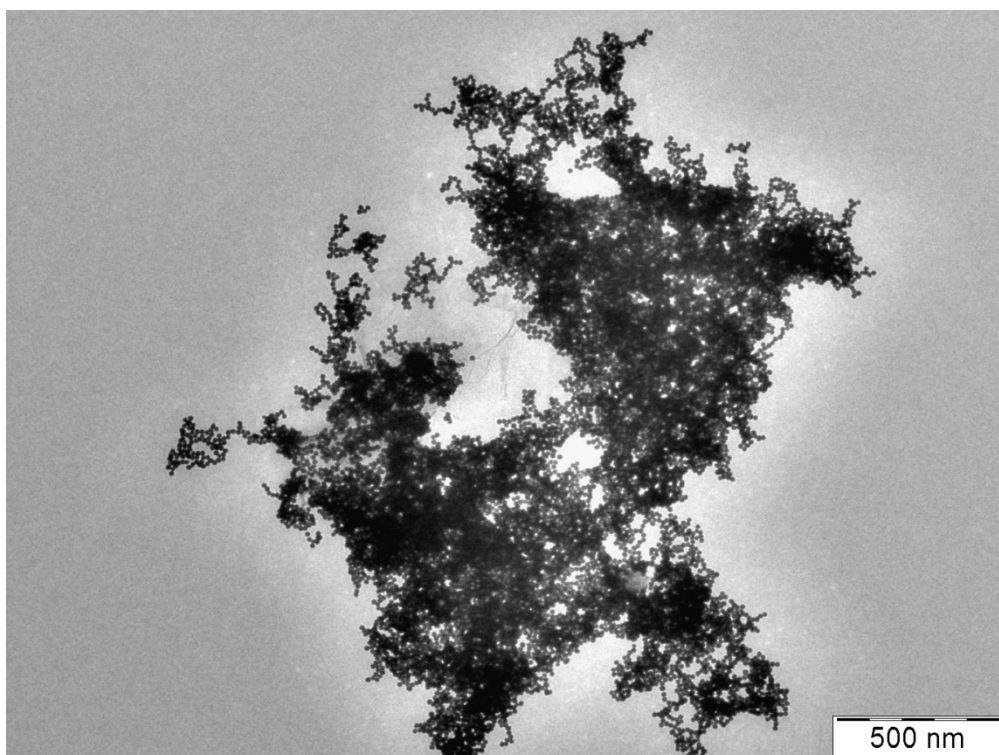


Figure 3. TEM images of 5-mercaptopethyltetrazole-capped gold NPs agglomerated under action of zinc acetate.

In summary, we have developed synthesis of stable water soluble noble metal NPs capped with tetrazoles. The optical properties of NPs obtained were found to be sensitive to different metal ions. Complexation of tetrazole-capped NPs was shown to be a convenient and facile method of assembling of NPs accompanied with drastic changes in plasmonic behavior. Future collaboration with host institution is planned. In particular, studies of sensitivity of tetrazole-capped NPs towards other metal ions are planned, which will be helpful for the construction of NPs aggregates with controllable structures and functions and for the improvement of the selectivity and sensitivity in the colorimetric detection of heavy metal ions by using NPs. Moreover, the metal gels obtained will be used for fabrication of corresponding aerogels, which are of interest in optical sensing, photovoltaics, LEDs, nonlinear optics, and catalysis [13]. The results obtained provide a basis for development of plasmonic nanosensors for determination of biologically active tetrazoles and other nitrogen heterocycles as well as metal ions.

The preliminary results of research are planned to report on International Workshop “Ordered and Non-Ordered Superstructures of Nanosized Objects: Preparation, Properties, Applications, and Modeling” (09 - 13 July 2012, Max Planck Institute for the Physics of Complex Systems, Dresden, Germany).

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