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A Versatile Strategy for Quantum Dot Ligand Exchange

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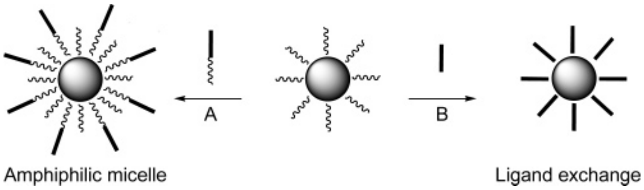
Colloidal nanocrystal quantum dots (QDs) are of great interest because of their unique size-dependent optical properties.[1] One of the major applications of these nanoparticles is their use as an alternative to fluorescent organic dyes.[2] However, the prerequisite for the development of QD-based bioimaging systems is to gain access to photostable, compatible, and water-soluble nanocrystals.[3] Most of the reported syntheses lead to QDs coated with hydrophobic molecules.[4] Two main strategies exist for converting hydrophobic QDs into hydrophilic ones. The first approach is based on the inclusion of hydrophobic QDs into amphiphilic micelles leading to an interdigitated bilayer[5] (Scheme 1, path A). The supramolecular assembly is, however, large (diameter >10 nm) and mainly maintained by local hydrophobic interactions. The second approach consists of exchanging of the original organic layer with hydrophilic ligands[6] (Scheme 1, path B). This strategy has successfully been applied using functional groups which strongly adhere to the QD surface, such as phosphines, amines, and thiols.

Thiols are by far the motifs which exhibit the strongest affinity for CdSe nanoparticles but suffer from a major drawback, i.e. instability toward oxidation.[7] This problem was recently circumvented using carbodithioate ligands,[8] which improved resistance of the nanocrystals against photooxidation. However, a specific and adapted synthesis is required each time new ligands are needed.

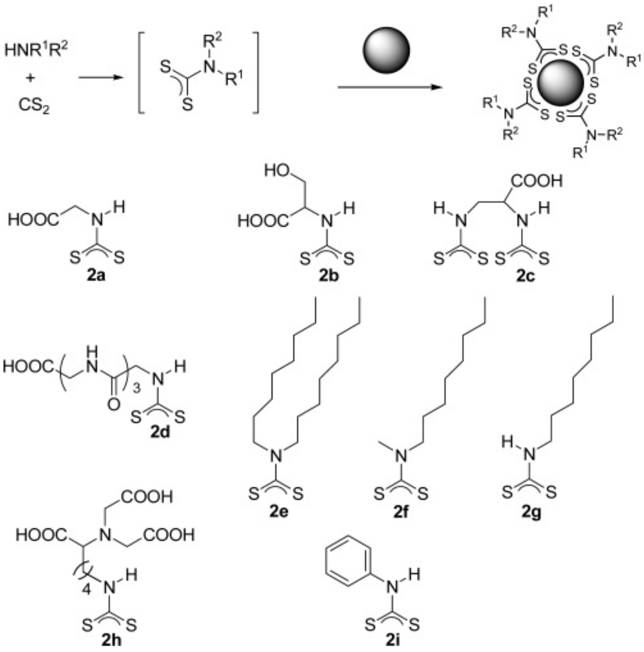
In this paper, we report an alternative method for the replacement of the original quantum dot ligands by dithiocarbamate moieties.[9] This process offers the advantage, over the classical approaches, in that the setup of the reaction is easy, by simply mixing carbon disulfide with the appropriate amine. Depending on the intrinsic nature of the substituents borne by the amino group, different properties are conferred to the nanocrystal, such as solubility in various solvents. Furthermore, as carbodithioates are bidentate chelating moieties which display high affinity for metal atoms, increased stability of the nanocrystal is expected.

Starting core−shell CdSe/ZnS nanocrystals were prepared using a modified reported process involving trioctylphosphine oxide (TOPO) as stabilizing agent (see Supporting Information for details). Initial ligand exchange experiments were conducted using amines bearing aliphatic or aromatic side chains (e.g., **2e**, **2f**, **2g**, **2i**) (Scheme 2). In a typical experimental procedure, QDs were precipitated in MeOH and redissolved in $CHCl_3$. Dioctylamine in excess was added, followed by an equimolar quantity of CS_2. The solution was stirred for 3 h at room temperature before the nanocrystals were precipitated again with MeOH. The supernatant was discarded, and the newly coated dithiocarbamate QD-**2e** was collected and could be dissolved in various organic solvents, such as $CHCl_3$, THF, etc.

Scheme 1



Scheme 2



To determine the fate of the original phosphine ligands upon exposure to dithiocarbamate **2e**, we carried out ^{31}P NMR measurements using PPh_3 as internal standard centered at 0 ppm. The starting QDs exhibited no NMR signal (Figure 1c). This is presumably due to the low concentration of the QDs in $CDCl_3$ but also to the inhomogeneous distribution of the magnetic environment which broadens the NMR signals.[10] However, after 3 h in the presence of CS_2 and dioctylamine, we observed a sharp peak at 48 ppm which corresponds to free TOPO that was released from the QD surface (Figure 1a). It is noteworthy that no ^{31}P signal was detected when either dioctylamine or CS_2 was reacted alone with the QD. This emphasizes the fact that ligand exchange occurred only upon exposure to the dithiocarbamate moiety. Furthermore, the ^1H NMR spectrum of the newly coated nanocrystals (Figure 1b) matches that of dithiocarbamate **2e** (Figure 1d) but key protons (i.e., $-CH_2-N-$) at ca. 4 ppm are shifted. This difference suggests strong interaction of **2e** with the QD surface.

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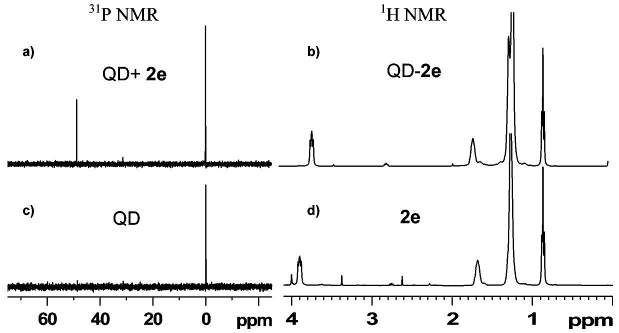

Figure 1. ^{31}P NMR of the QD before (c) and after (a) ligand exchange. ^{1}H NMR of dithiocarbamate **2e** (d) and of QD coated with **2e** (b).

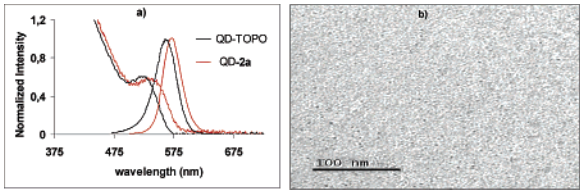

Figure 2. (a) Absorption and fluorescence spectra (excitation wavelength 350 nm) before and after ligand exchange. (b) TEM of QD-**2a**.

The photoluminescence profile of the newly coated core−shell quantum dots depended greatly on the thickness and the type of the shell grown on the CdSe core. We observed complete quenching or strong decrease of the fluorescence when core-only or QDs coated with thin layers of ZnS were used. On the contrary, when multilayer CdSe/CdS/CdZnS/ZnS QDs (see Supporting Information) were used, the photoluminescence spectra remained mostly unchanged upon ligand exchange with the dithiocarbamate moiety. The quality of the shell is therefore essential for the preservation of the QD optical properties.

The ligand exchange technique that we have developed is not limited to the grafting of hydrophobic ligands. It can easily be applied to make QDs water soluble. To convert hydrophobic nanocrystals into hydrophilic ones, we chose amino acid-based ligands as the amino group could serve as an anchoring moiety via its interaction with CS_2 while the carboxylic group induces aqueous solubility. Further derivatization of the coated QD can also be envisioned through chemical coupling to the carboxylate.

The core−shell nanocrystals were thus coated with amino acids using a slightly modified process. A typical procedure is given for the preparation of QD-**2a**. Hydrophobic QDs were first precipitated in MeOH and redissolved in 1:1 MeOH/$CHCl_3$. In a separate flask, a solution of glycine in the same solvents was reacted with tetramethylammonium hydroxide and CS_2. To the latter is added the QD solution, and the mixture is stirred at room temperature for 12 h. Diethylether is then added, and the precipitate is isolated by centrifugation. The resulting solid is finally dissolved in pH 8.5 Tris buffer and characterized.

Spectroscopic analyses (Figure 2a) of the nanocrystals indicated a 10 nm bathochromic shift in both fluorescence and absorption spectra compared to that of TOPO-QDs. This ligand exchange yielded single water-soluble QDs that remained well dispersed in solution as confirmed by transmission electron microscopy (Figure 2b). The photoluminescence intensity of the nanocrystals was compared before and after surface modification. Fluorescence measurements after exchange of ligands indicated a drop of ca. 40% in quantum yield. This behavior has already been observed in aqueous systems and commented on by others.[11] Photostability studies were also undertaken by flashing UV light through an aqueous QD solution. After 500 consecutive illuminations at 350 nm (4 s each), the glycine-coated nanocrystal **2a** still exhibited 85% of the initial fluorescence intensity and no difference in absorbance was observed. The effect of a saline solution (up to 1 M [NaCl]) was also investigated, showing no changes in the photoluminescence properties of the quantum dot. Taken together, these results demonstrate that the coating of the nanocrystals is robust under harsh conditions, as photobleaching is slow and concentrated sodium chloride has no effect on the optical properties.

The same ligand exchange procedure was extended to more complex amino acid systems such as serine (**2b**), tetraglycine (**2d**), nitrilotriacetic acid (**2h**), and 2,3-diaminopropionic acid (**2c**). In the latter case, double anchoring on the nanocrystal surface is achieved.

In summary, we report here a new and efficient procedure for ligand exchange on core−shell nanocrystals. The process developed above involves the reaction of carbon disulfide with an amine-containing ligand. The resulting dithiocarbamates are strongly bound to the surface of the quantum dots, leading to a secure coating of the nanoparticle.

Supporting Information Available: Experimental details and spectroscopic characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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