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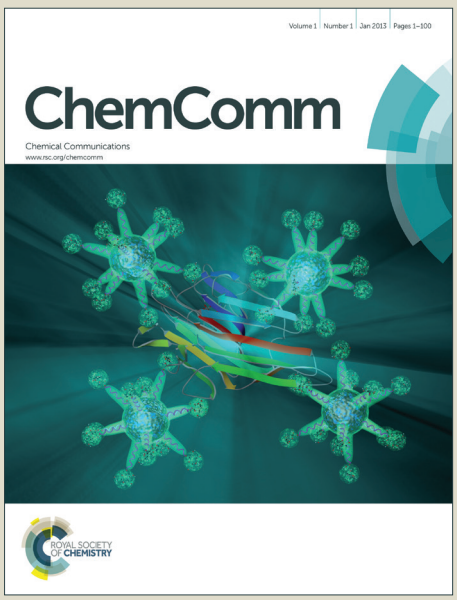

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COMMUNICATION

Modulation of the solubility of luminescent semiconductor nanocrystals through facile surface functionalization

Cite this: DOI: 10.1039/x0xx00000x

Received ooth January 2012,
Accepted ooth January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

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The solubility of luminescent quantum dots in solvents from hexane to water can be finely tuned by the choice of the countercations associated with carboxylate residues present on the nanocrystal surface. The resulting nanocrystals exhibit long term colloidal and chemical stability and maintain their photophysical properties.

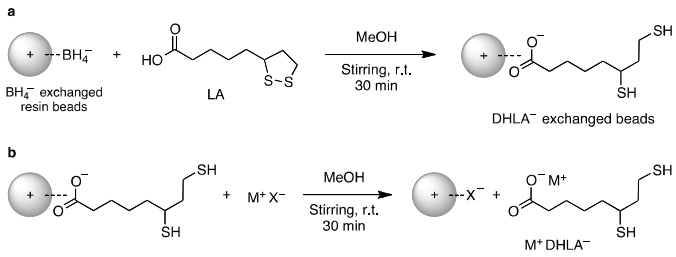
Quantum dots (QDs) are semiconductor nanocrystals endowed with unique size-dependent optical and electronic properties[1] and are emerging as substitutes for molecular fluorophores[2] for applications in chemo/biosensing,[3] medical diagnostics and therapy,[4] light-emitting devices,[5] and solar cells.[6]

Despite recent progress in the preparation of high quality QDs in aqueous media,[7] most reliable and widely used synthetic approaches are based on reactions performed in organic solvents.[1] Such methods enable the preparation of QDs with accurate control of their size and properties and afford nanocrystals whose surface is coated with a layer of highly hydrophobic molecular ligands.[8] These QDs are, therefore, (moderately) soluble only in apolar organic solvents such as toluene, hexane or chloroform. However, several applications – particularly, bioimaging and medical therapy – require that the nanocrystals are compatible with, and soluble in, aqueous media. Encapsulation of QDs with amphiphilic polymers[9] results in stability in water and preserves the photophysical properties, but the increased diameter of the encased nanoparticles is a limitation for biological and FRET applications.[3,4] Furthermore, utilization in optoelectronic devices requires that the QDs are soluble in suitable solvents for the deposition of homogeneous thin films, or that they are miscible with charge transporting host materials.

The control of the solubility of QDs in common solvents is crucial for viable processing of these nanomaterials. A frequently used methodology involves the replacement of the native capping ligands with other ligands that combine a surface anchoring unit with a functional (e.g., hydrophilic) module.[3,4] Although exceptions exist,[10] ligand-exchanged QDs usually exhibit a degradation of the photophysical properties and a poor long-term chemical and photochemical stability.[11] Ligands with multiple thiol anchoring groups, such as dihydrolipoic acid (DHLA) and related compounds, have become increasingly popular, owing to their ability to form robust capping monolayers on the surface of metal and semiconductor nanocrystals.[12] DHLA is obtained from lipoic acid (LA) upon reductive cleavage of the S–S bond of its 1,2-dithiolane moiety. While such a reaction occurs spontaneously in the presence of a noble metal surface, LA must be chemically reduced to DHLA[12] or UV-irradiated[13] prior to adsorption to semiconductor QDs.

Here we describe a general route for converting LA-based ligands to the active DHLA derivatives and using them to replace the native caps of QDs. The procedure enables the phase transfer of the nanocrystals in polar and aqueous media and, if LA is used as the capping agent, a facile adjustment of their solubility in a wide range of solvents.[14]

The method relies on the use of a borohydride-loaded ion-exchange resin[15] for the reduction of the 1,2-dithiolane, as shown in Scheme 1. The resin is commercially available or can be prepared by stirring an aqueous solution of $NaBH_4$ with an anion exchange resin (e.g., Amberlite® IRA-400).[16] In our case the resin contained typically 2.5 mmol of BH_4^- per gram of polymer. The addition of the resin beads to a MeOH solution of lipoic acid (BH_4^-/LA ≈ 2:1) led, after 30 min stirring, to the conversion of LA to the $DHLA^-$ anion (Scheme 1a). The process can be conveniently followed by absorption spectroscopy, monitoring the decrease of the disulfide band of lipoic acid at 330 nm. These measurements also suggest that DHLA is chemisorbed on the resin, most likely because of the interaction between the carboxylate and the ammonium moieties of the resin (Scheme 1a).[†]



Scheme 1 Reduction of lipoic acid with a borohydride exchanged resin (a) and extraction of $DHLA^-$ from the resin beads (b).

In order to extract the $DHLA^-$ species from the resin, we treated the beads with a MeOH solution containing an excess of a metal or ammonium salt (M^+X^-, Scheme 1b). The X^- anion displaces $DHLA^-$ from the resin (which can be subsequently recovered), and a MeOH solution containing the active ligand as its M^+ salt is obtained. It should be pointed out that the purification procedures[12] usually carried out after the reduction of LA are not needed. At the end of the reaction, the excess reactant can be easily removed from the solution by decantation of the resin. The amount of DHLA just necessary for the cap exchange may be prepared, thus avoiding the storage of stock solutions of ligand under inert atmosphere at low temperature.

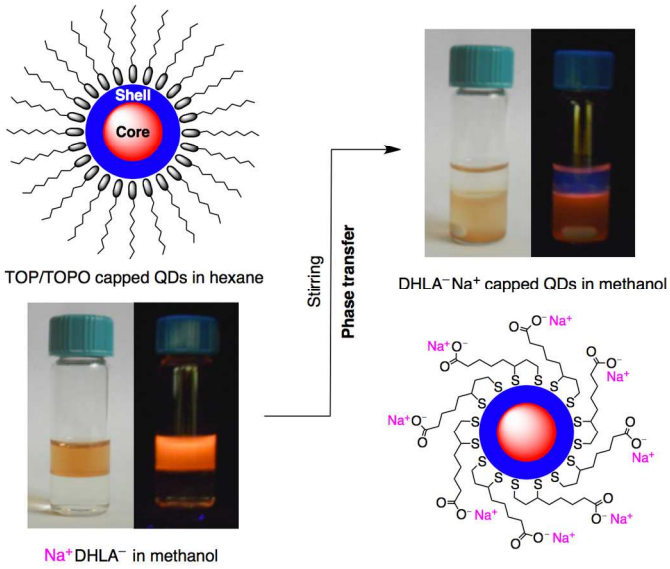


Fig. 1 Transfer of the hydrophobic QDs in a polar solvent driven by cap exchange with $DHLA^-$ ligands. The images refer to CdSe-5ZnS nanocrystals (d_{core} = 3.6 nm).

The cap exchange was performed by adding a hexane solution containing the hydrophobic QDs capped with trioctylphosphine (TOP) and trioctylphosphine oxide (TOPO) to the $DHLA^-Na^+$ ligand, obtained using NaOH as the M^+X^- species in Scheme 1b, in methanol. Upon stirring the biphasic mixture, a color change indicative of phase transfer of the QDs to methanol was readily observed (Fig. 1), indicating a fast and efficient ligand exchange. Alternatively, the hydrophobic QDs were added as a solid to the DHLA solution; in this case the cap exchange caused the rapid dispersion of the nanocrystals in the MeOH. After removal of the colorless hexane layer (if present) the MeOH suspension was washed with fresh hexane to take away any trace of hydrophobic ligands and unreacted nanocrystals. The methanol was then evaporated under vacuum and the dried $DHLA^-Na^+$ QDs were dissolved in water and purified.[†]

Typically, 5-10 μM aqueous solutions of $DHLA^-Na^+$ capped nanocrystals of different structure and size were obtained, which resulted to be stable for at least 3 months. The minor shift in the absorption and emission peak wavelengths with respect to the starting QDs (Fig. 2) indicates that no aggregation takes place. In line with literature reports,[17] CdSe cores were not emissive after phase transfer, whereas the luminescence efficiency of the final core-shell QDs in aqueous solution was 30-50% of that of the native hydrophobic nanoparticles.[†]

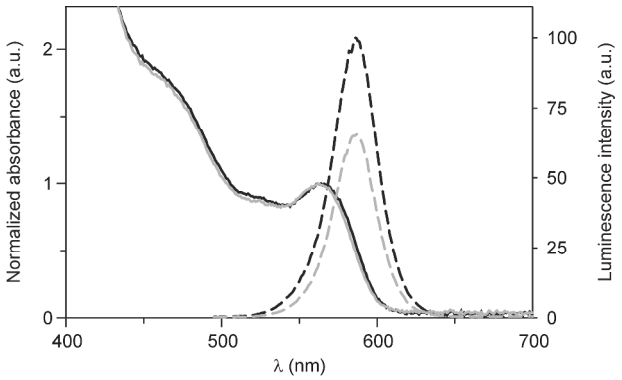


Fig. 2 Absorption (full line) and emission (dashed line; λ_{exc} = 485 nm) spectra of CdSe-3ZnS QDs (d_{core} = 3.4 nm) TOP/TOPO capped in $CHCl_3$ (black) and $DHLA^-Na^+$ capped in H_2O (grey).

Activation with the resin was also effective for a ligand comprising a 1,2-dithiolane moiety attached to a hydrophilic poly(ethylene glycol) domain (LA-PEG_{400})[12] and phase transfer of QDs was observed.[†] In such a case the reduced DHLA-based ligand did not bind to the resin and the extraction step described in Scheme 1b was not necessary.

Interestingly, we found that the nature of the M^+X^- species not only plays the important role of extracting $DHLA^-$ from the resin (Scheme 1b) but also determines the solubility of the final QDs. We performed several cap exchange reactions following the above described route and using different metal or ammonium salts or hydroxides in place of NaOH. As shown in Table 1, QDs capped with the same ligand ($DHLA^-$) and different cations exhibit remarkably different solubility properties. Counterion effects in nanocrystals capped with ionic ligands have been studied[18] but, to our knowledge, this is the first investigation highlighting the role of counterions for adjusting the QD solubility in polar solvents. The spectroscopic properties of the nanocrystals are maintained in all the dispersions listed in Table 1, with absorption and emission peaks shifts not exceeding 5 nm in comparison to the native QDs. As an example, Fig. 3 shows photographs of QDs capped with $DHLA^-TBA^+$ in different solvents.

Although a rationalization of the pattern shown in Table 1 is not straightforward, the solubility of the $DHLA^-M^+$ QDs in which M^+ is an alkali cation or a quaternary ammonium ions with short alkyl substituents (e.g. TMA^+) in methanol or water can be explained considering the large solvation enthalpies of these cations in these solvents. Tetraalkylammonium ions with longer chains render the QDs compatible with less polar organic solvents, owing to Van der Waals forces between the solvent molecules and the alkyl chains. Other effects can be relevant in specific cases: for example, favorable

Table 1 Solubility of CdSe-3ZnS QDs capped with $DHLA^-$ and different M^+ countercations in various solvents at room temperature.[a]

Solvent (ε^b)	Hexane (1.89)	Toluene (2.38)	$CHCl_3$ (4.81)	THF (7.58)	Acetone (20.7)	MeOH (32.7)	MeCN (35.9)	DMSO (46.5)	Water (80.2)
Li^{+c}	✗	●	●	✗	✗	✗	✗	✗	●
Na^{+c}	✗	✗	●	●	✗	✗	✗	✗	●
K^{+c}	✗	✗	✗	✗	✗	●	✗	✗	●
TMA^{+c}	✗	✗	✗	✗	✗	●	✗	●	●
$TEA^{+d,e}$	✗	✗	✗	✗	✗	●	●	✗	●
TBA^{+c}	✗	✗	●	●	●	●	●	●	●
TOA^{+e}	✗	✗	✗	✗	✗	●	✗	✗	✗
CTA^{+f}	●	●	●	●	✗	✗	✗	✗	✗
Native QDs[g]	●	●	●	●	✗	✗	✗	✗	✗

[a] Green circles indicate that the QDs form homogeneous solutions at 0.5-1.0 μM concentrations; red crosses denote insoluble samples. TMA^+, Tetramethylammonium; TEA^+, tetraethylammonium; TBA^+, tetra(*n*-butyl)ammonium; TOA^+, tetra(*n*-octyl)ammonium; CTA^+, cetyltrimethylammonium. [b] Relative dielectric constant. [c] $X^- = OH^-$. [d] $X^- = ClO_4^-$. [e] $X^- = NO_3^-$. [f] $X^- = Br^-$. [g] As synthesized nanocrystals capped with TOP/TOPO ligands.

cation-π interactions of lithium ions with aromatic solvent molecules may explain why $DHLA^-Li^+$ QDs are soluble in toluene. It is noteworthy that TBA^+ ions provide solubility of the anionic nanocrystals in a large variety of solvents (Table 1), suggesting that such cations can afford a good compromise in terms of lattice and solvation energies in media as different as chloroform and water.

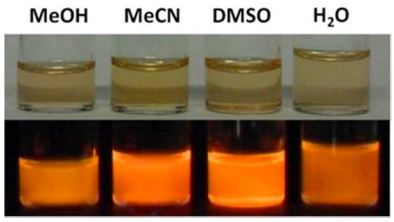


Fig. 3 Photographs of 0.5 μM CdSe-5ZnS QDs (entry 6 in Table 1) capped with $DHLA^-TBA^+$ in different solvents under ambient light (top) and UV light (λ_{exc} = 365 nm, bottom).

In summary, we have developed a simple method for the chemical activation of ligands based on the 1,2-dithiolane unit and their utilization for exchanging the native capping ligands of QDs. If the ligand is lipoic acid, the procedure enables the precise modulation of the QD solubility in a wide range of solvents with different polarity (from hexane to water). The final nanocrystals maintain their spectroscopic properties and exhibit long term colloidal and chemical stability. Indeed, the development of viable routes to program the solubility of QDs in common solvents without degrading their physical properties is an important requirement to foster the technological exploitation of these nanomaterials.

The authors acknowledge support from the EU (FP7-NMP project Hysens, No. 263091), MIUR (PRIN 2010CX2TLM), the University of Basel and the University of Bologna.

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† Electronic Supplementary Information (ESI) available: materials, synthetic procedures, photophysical data. See DOI: 10.1039/c000000x/

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