Lanthanide-Doped $NaYF_4$ Nanocrystals in Aqueous Solution Displaying Strong Up-Conversion Emission

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$NaYF_4$:Yb^{3+},Er^{3+} nanocrystals showing high colloidal solubility in water have been obtained by treating the nanocrystals with 1-hydroxyethane-1,1-diphosphonic acid (HEDP). HEDP attaches to the surface of the nanoparticles and leads to well-separated particles in aqueous solution as verified by IR spectroscopy and dynamic light scattering measurements. In addition, the surface modification with HEDP increases strongly the up-conversion efficiency of powders and aqueous colloidal solutions of the nanocrystals. These attractive features, above all the hydrophilic nature of the nanoparticles, should make them suitable especially for bio-applications.

Introduction

Luminescent nanocrystals have attracted a great deal of attention for their potential wide range of applications including display devices,[1] lasers,[2] and biological imaging agents.[3−9] More recently, a new subgroup of these materials has been developed, which are capable of converting long wavelengths radiation into shorter wavelengths and which therefore offer new opportunities for biological labeling applications.[10−13] The emission of these materials is based on the up-conversion process where the energy of two or more IR photons is transferred to one lanthanide dopant ion, resulting in excitation of this ion into a 4f state at high energy. If two photons are involved, excitation into the $^4F_{7/2}$ state at about 20500 cm^{-1} occurs. Visible luminescence is emitted when the ion subsequently relaxes to the ground state. In contrast to second harmonic generation (SHG) and simultaneous two-photon absorption (STPA), the up-conversion process involves metastable quantum mechanical states only.[18] Consequently, the efficiency at low excitation densities is orders of magnitude higher than that for second harmonic generation and simultaneous two-photon absorption. Typical excitation densities fall in the range of $1-10^3$ W cm^{-2} for up-conversion, compared to 10^6-10^9 W cm^{-2} for STPA.[13−15] At very high excitation densities, on the other hand, saturation is observed for the up-conversion emission because the concentration of dopant ions in the material is limited.

The most efficient up-conversion materials known today are based on fluorides which are doped with Yb^{3+} and Er^{3+} or Yb^{3+} and Tm^{3+} ions.[16,17,26] In these materials the excitation light is primarily absorbed by Yb^{3+}, showing a higher absorption at 975 nm. In the case of Yb^{3+}/Er^{3+} co-doping, the energy of two excited Yb^{3+} states is then transferred to one Er^{3+} ion, resulting in emission mainly in the green and the red spectral region. In the case of Yb^{3+}/Tm^{3+} the energy of four excited Yb^{3+} states is transferred to one Tm^{3+} ion and emission of blue and violet light is observed. In general, efficient hosts for photon up-conversion are based on materials with low phonon energies which minimize non-radiative multiphonon relaxation processes in the dopant. The best host material known today for these ions is $NaYF_4$ in its hexagonal phase (β-phase).[16,17,19] In 2004 we reported the successful synthesis and intense multicolor up-conversion emission of transparently dispersed cubic phase (α-phase) $NaYF_4$ nanocrystals doped with Yb^{3+}/Er^{3+} and Yb^{3+}/Tm^{3+}.[18] Since then also nanocrystals of the β-phase have been synthesized and their up-conversion emission in colloidal solution was investigated.[19]

To be suitable for biolabeling applications, however, the nanocrystals must be soluble in aqueous media. In this paper

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we therefore present a surface modification procedure which renders $NaYF_4$ nanocrystals soluble in water.

Experimental Section

Synthesis. *Synthesis of $NaYF_4$:Yb^{3+},Er^{3+} Nanocrystals.* $NaYF_4$: 28.4% Yb, 2.9% Er nanocrystals were prepared in the coordinating solvent *N*-(2-hydroxyethyl)ethylenediamine (HEEDA) similar to the method previously described.[18] The following three solutions were used in the synthesis.

(A) Solution of the Lanthanide Chlorides. A clear solution of 2.12 g (6.99 mmol) of $YCl_3 \cdot 6H_2O$ (99.9%, Treibacher Industries), 1.12 g (2.89 mmol) of $YbCl_3 \cdot 6H_2O$ (99.9%, Treibacher Industries), and 0.11 g (0.29 mmol) of $ErCl_3$ (99.9%, Treibacher Industries) in about 20 mL of methanol was combined with 20 mL of *N*-(2-hydroxyethyl)ethylenediamine (99%, Sigma Aldrich) and 42 mL of diphenylether. The methanol was removed with a rotary evaporator, and the water was distilled off in high vacuum at 75 °C. The remaining slightly cloudy suspension was allowed to cool down to 60 °C and was kept at this temperature under dry nitrogen.

(B) Preparation of the Sodium Alkoxide Solution. A solution of the sodium alkoxide of *N*-(2-hydroxyethyl)ethylenediamine (HEEDA) was prepared by dissolving 0.23 g (10 mmol) of sodium metal in 10 mL of HEEDA at 45 °C under dry nitrogen.

(C) Preparation of the Fluoride-Containing Solution. NH_4F (1.46 g, 39.4 mmol) (98% Fluka) was dissolved in about 20 mL of methanol and combined with 20 mL of HEEDA. The methanol was removed with a rotary evaporator at 45 °C and subsequently in high vacuum at 60 °C. The remaining solution was kept at 45 °C under dry nitrogen.

Synthesis of the Nanocrystals. Solution A and solution B were combined and heated to 60 °C. Subsequently, the fluoride-containing solution (**C**), which had a temperature of 45 °C, was added under stirring and the resulting mixture was degassed at 80 °C under vacuum. The reaction mixture was heated to 185 °C under dry nitrogen and kept at this temperature for 13 h. After the transparent solution had cooled down to room temperature, the nanocrystals were precipitated by adding a mixture of 200 mL of water and 200 mL of propanol. The precipitate was separated by centrifugation and washed several times by repeatedly re-suspending the solid in 2-propanol and centrifuging the suspension. Usually, the purified precipitate was directly re-dispersed in ethanol without drying the powder (see below). For XRD measurements the precipitate was dried in air (white powder, yield: 1.72 g (79%)).

Colloidal Solution in Ethanol. Directly after the particles were washed with propanol, the purified particles were re-dispersed in ethanol. The suspension, containing approximately 1 wt % of nanocrystals was heated to 70 °C for 10 min, allowed to cool, and subsequently treated in an ultrasonic bath for 12 min. DLS measurements indicated that the nanocrystals in the weakly opalescent solution contained agglomerates, the agglomerates having a size of approximately 80 nm (Figure 4).

Surface Modification of $NaYF_4$ Nanocrystals with 1-Hydroxyethane-1,1-diphosphonic Acid (HEDP). The purified $NaYF_4$ nanocrystals were re-dispersed in HEEDA by adding a solution of 1.58 g (7.38 mmol) of $NaYF_4$:28.4% Yb, 2.9% Er in 198 mL of ethanol (prepared as described before) to 70 mL of HEEDA at ambient temperature and subsequently removing the ethanol with a rotary evaporator. To the resulting transparent colloid a solution of 2 g (9.7 mmol) of HEDP (95%, containing 2% H_2O, Monsanto) in 15 mL of HEEDA was added at room temperature and the combined solution was heated to 60 °C for 4 h. The modified nanocrystals were precipitated by adding 200 mL of propanol to the transparent reaction mixture. After centrifugation, the supernatant solution was discarded and the precipitate was re-suspended in propanol. After treatment of the suspension for 15 min in an ultrasonic bath, the precipitate was again centrifuged and the supernatant discarded. This washing procedure was repeated seven times. Finally, the nanoparticles were isolated by removing the propanol with a rotary evaporator and the white residue was dried under vacuum. This leads to $NaYF_4$ nanocrystals with HEDP and HEEDA attached to their surface ($NaYF_4$:Ln$\cdot$$HEDP_{RT}$).

Removal of HEEDA: Synthesis of $NaYF_4$:Ln$\cdot$$(HEDP)_{180}$ and $NaYF_4$:Ln$\cdot$$(HEDP)_{320}$. The HEEDA content of the $NaYF_4$:Ln$\cdot$$HEDP_{RT}$ particles was distilled off in vacuum ($p < 0.1$ mbar) at 180 or 320 °C. A hot air gun was used to heat the white substance at 180 or 320 °C. $NaYF_4$:Ln $(HEDP)_{180}$ and $NaYF_4$:Ln $(HEDP)_{320}$ were isolated as transparent, hard, and glassy substances. Heating at 320 °C leads to a ratio between $NaYF_4$: Ln and HEDP of approximately 0.1. The two materials could be very easily dispersed in water to yield transparent aqueous solutions.

Characterization: XRD and Up-Conversion Luminescence Measurements. The X-ray diffraction data of nanocrystal powders were recorded with a X'Pert Pro Diffractometer (Panalytical). Up-conversion emission spectra of colloidal solutions of the nanocrystals were measured with a Fluorolog 3 spectrometer (Jobin Yvon) combined with a continuous wave laser diode (Infineon SPL2F98). Quartz cuvettes (Hellma, QX) containing the samples were placed inside the spectrometer and excited by the 975 nm light of the laser diode via an optical fiber. All spectra were corrected for the sensitivity of the monochromator and the detection system. The up-conversion emission spectra of powder samples were measured similarly but in front-face geometry. Dynamic light scattering measurements were performed with the Nanosizer (Malvern).

Results and Discussion

Particle Synthesis and Purification. The synthesis in the coordinating solvent *N*-(2-hydroxyethyl)ethylenediamine (HEEDA) yields particles of the cubic α-phase as verified by X-ray powder diffraction (Figure 1a). From the width of the diffraction peaks a mean particle diameter of approximately 26 nm is calculated, a value which is in accord with the size distribution observed in TEM images of the particles (Figure 1b).

The coordinating solvent HEEDA is miscible with water in any portion, but the addition of water to a colloidal solution of $NaYF_4$ nanoparticles in HEEDA nevertheless leads to precipitation of the nanocrystals. We used this property of the colloidal solution to separate the particles from the byproducts of the reaction.

When the precipitate was washed extensively with 2-propanol/water (see Experimental Section for details), HEEDA was removed from the surface of the particles as was verified by thermogravimetric measurements (TG) and IR spectrosopy. TG measurements of the nanoparticles purified by washing show that the loss of mass upon heating to 500 °C is smaller than 5%, despite the large surface-to-volume ratio of the particles (Figure 2). The TG analysis is in accord with the IR spectrum of the purified nanocrystals (Figure 3), which displays no strong absorption peaks between 4000 and 500 cm^{-1}. The purified nanocrystals, which cannot be dispersed in water, can be redispersed in pure HEEDA as given in the Experimental Section.

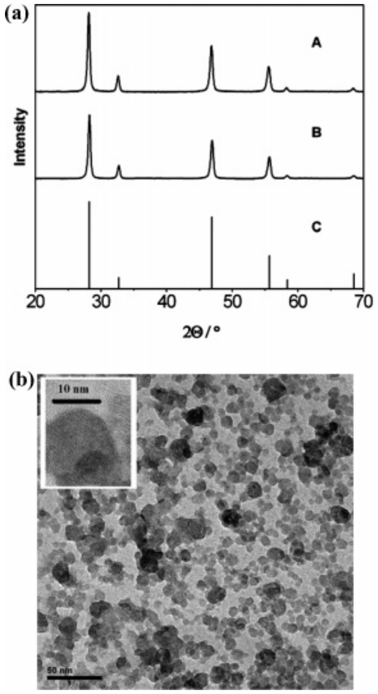

Figure 1. (a) X-ray diffraction pattern from (A) $NaYF_4$:Ln $(HEDP)_{320}$ nanocrystals, (B) $NaYF_4$:Ln nanocrystals, and (C) calculated line pattern for the α-$NaYF_4$ structure (cubic, space group *Fm*3*m*, ICSD collection code 60257). (b) TEM image of $NaYF_4$:Ln nanocrystals. Inset: high-resolution image of a nanocrystal.

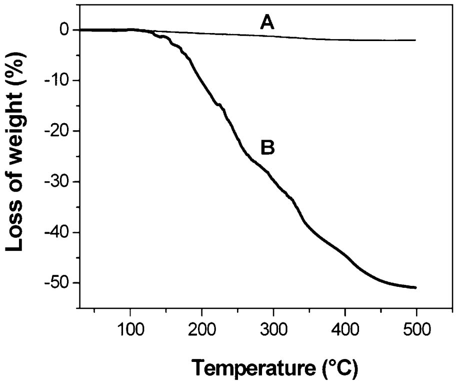

Figure 2. TG curves of (A) $NaYF_4$:Ln nanocrystals and (B) $NaYF_4$:Ln $(HEDP)_{RT}$ nanocrystals.

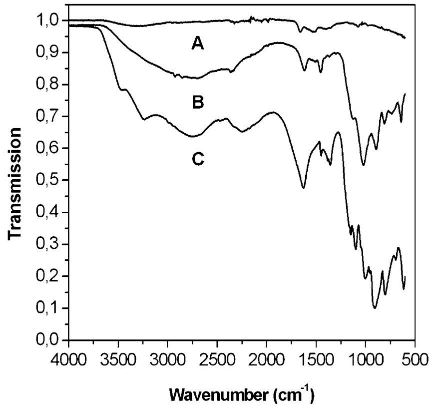

Figure 3. IR spectra of $NaYF_4$:Ln nanocrystals (A) and $NaYF_4$:Ln $(HEDP)_{320}$ nanocrystals (B) compared with free HEDP (C).

Surface Modification with Hydroxyethyldiphosphonic Acid. To render the nanocrystals soluble in water, their surface was modified by treating the particles in colloidal solution with 1-hydroxyethane-1,1-diphosphonic acid (HEDP). HEDP is a strong tetraprotonic acid which is highly soluble in water and in HEEDA. Since both the acid and the nanocrystals are soluble in HEEDA, the surface reaction can take place in solution, i.e., under conditions where most of the surface area of the particles is accessible. HEDP is known to form strong complexes with divalent and trivalent cations.[20,21] In a previous paper, we have used HEDP to increase the colloidal stability of hydrothermally prepared YVO_4: Eu nanoparticles in water,[22] indicating that the molecule also binds to atoms at the surface of nanocrystals.

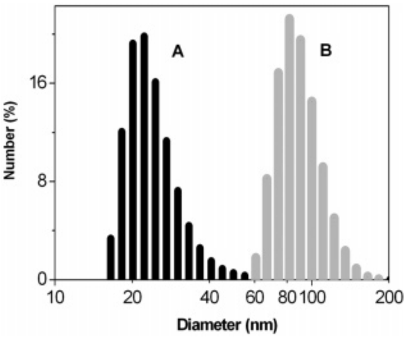

Figure 4. Characterization by dynamic light scattering: Particle size and size distribution in solution. (A) $NaYF_4$:Ln $(HEDP)_{RT}$ nanocrystals in water and (B) $NaYF_4$:Ln nanocrystals in ethanol.

As a strong acid, HEDP forms ionic compounds with HEEDA by protonating the amino groups of the solvent. In fact, we observed that after the reaction with HEDP the HEEDA at the surface of the nanoparticles is not easily removed by washing anymore. Even after extensive rinsing, the TG curve of the treated nanoparticles shows a significant loss of mass upon heating to 500 °C (Figure 2). However, since ammonium salts are thermally unstable compounds, HEEDA can be removed from the particle surface by vacuum distillation at temperatures above 180 °C (see Experimental Section for details). The diphosphonic acid (HEDP) remains on the particle surface as is verified by IR spectroscopy (Figure 3). The residue obtained after vacuum distillation is highly soluble in water. Dynamic light scattering measurements (Figure 4) indicate a particle size in water of approximately 24 nm, well in accord with the mean particle size observed in the TEM and the size calculated from the XRD data.

The XRD patterns recorded before and after the surface modification are very similar (Figure 1a), indicating that the crystal phase and the domain size are not affected by the treatment with HEDP.

The high solubility of the particles in water is accompanied by a strong decrease of their solubility in organic solvents. Even in polar organic solvents like ethanol, the solubility is very low, indicating a highly polar particle surface due to the presence of HEDP. Before the surface treatment the particles are soluble in ethanol, albeit the particles are not very well separated in this solvent, as is evident from dynamic light scattering measurements (Figure 4).

It is noteworthy that the high solubility in water is already achieved after the reaction of the nanocrystals with HEDP, without the necessity to remove the HEEDA by vacuum distillation. However, the high temperatures applied during

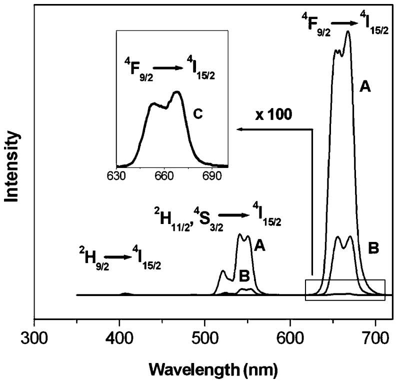

Figure 5. Emission spectra from NaYF$_4$:Ln (HEDP)$_{320}$ nanocrystals (A) and from NaYF$_4$:Ln (HEDP)$_{180}$ nanocrystals (B) compared with NaYF$_4$:Ln nanocrystals treated at 180 °C and without heat treatment (C).

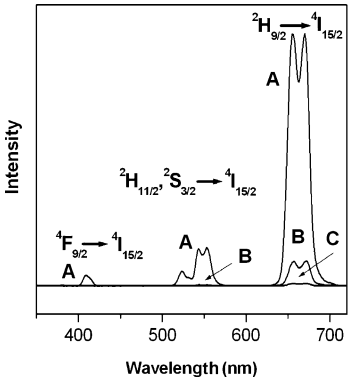

Figure 6. Emisson spectra of aqueous solutions. Solution of NaYF$_4$:Ln (HEDP)$_{320}$ nanocrystals (A). Solution of NaYF$_4$:Ln (HEDP)$_{RT}$ nanocrystals (C) and (B) (×10).

Figure 7. Photograph of the up-conversion luminescence in 2 wt % colloidal solutions of nanocrystals in water excited at 975 nm (invisible) with a laser power density of about 150 W cm^{-2}.

the vacuum distillation significantly improve the optical properties of the HEDP modified nanocrystals as will be discussed in the next paragraph.

Optical Properties. It is well-known that the quantum yield of luminescent nanoparticles is strongly affected by surface properties of the particles. In the case of lanthanide-doped materials the quantum yield and, hence, also the up-conversion efficiency can be strongly reduced if OH-, NH$_2$-, or other groups with vibrational modes of high energy are located in close proximity to the lanthanide ions. Therefore, the surface ligands and the solvent strongly affect the optical properties of these nanomaterials.

A strong effect on the up-conversion efficiency is caused also by the surface modification with HEDP. Figure 5 shows that the lowest up-conversion efficiency is observed for the purified NaYF$_4$ particles before surface modification. The low quantum yield in this case cannot be attributed solely to the presence of HEEDA, a likely quencher of the Yb^{3+} and Er^{3+} excited states, since most HEEDA has been removed from the surface by extensively washing the particles with propanol/water (see above). After surface modification of these particles with HEDP and removal of the HEEDA by vacuum distillation at 180 °C, the integrated emission intensity increases by a factor of approximately 45. However, it is not the elevated temperature alone that causes this increase because if the purified particles are heated to 180 °C under vacuum without the treatment with HEDP, the up-conversion efficiency is not affected. Obviously, the presence of HEDP on the particle surface is required to increase the luminescence intensity. Moreover, the emission intensity increases by an additional factor of approximately 4, if the vacuum distillation to remove the HEEDA is performed at 320 °C instead of 180 °C. This seems to indicate that at elevated temperatures a reaction takes place between HEDP and the particle surface, which reduces the number of surface sites where radiationless processes take place.

To exclude any influence of the surface roughness or the packing density which might affect the spectroscopic results obtained with nanocrystal powders, we also investigated the up-conversion efficiency in aqueous solution. The concentration of particles in each solution was adjusted such that the absorbance and the excitation wavelength had an identical value of 0.025 for all solutions. Figure 6 displays the up-conversion emission spectra of HEDP-modified nanocrystals before and after the vacuum distillation at 320 °C. Similar to the results obtained with powders, an increase by 2 orders of magnitude is observed for the integrated emission intensity after vacuum distillation at 320 °C. Consequently, the emission of the surface-modified particles in aqueous solution is quite intense, as is shown in Figure 7. Note that an inexpensive 1.5 W laser diode was used for taking the image and that the 975 nm excitation light was not focused. The power density at the end of the optical fiber was approximately 150 W cm^{-2}. The figure shows that the emitted light appears red to the eye instead of yellow-green as known from the emission of the bulk material. The reddish color is caused by the very low green-to-red ratio (GRR) of the up-conversion emission of our NaYF$_4$ nanocrystals. The GRR value is defined as the intensity ratio between the emission bands centered at about 550 and 670 nm and has been investigated by several groups.[16,19,23−25] For micrometer-sized hexagonal NaYF$_4$:Yb,Er, Krämer and Güdel et al. determined GRR values between 1.9[23] and 5.[16] An even higher GRR value of approximately 12 was reported by Huang and Meng.[25] Figure 8 shows that the GRR values of powders of our nanocrystalline samples are not even close to these values. Even after surface modification with HEDP the GRR value is as low as 0.227. Particles with lower up-conversion efficiency generally also show a lower GRR value. If the

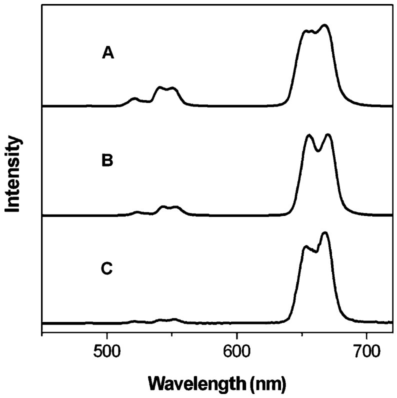

Figure 8. Green/red ratio of the crystals: (A) $NaYF_4$:Ln $(HEDP)_{320}$ GRR = 0.229. (B) $NaYF_4$:Ln $(HEDP)_{180}$ GRR = 0.109. (C) $NaYF_4$:Ln without heat treatment GRR = 0.045.

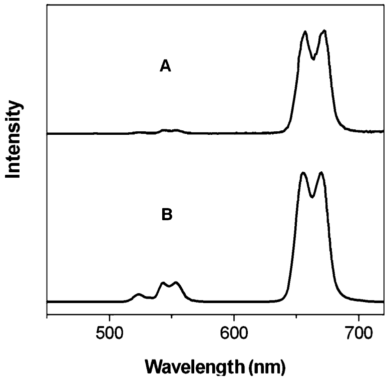

Figure 9. Green/red ratio in aqueous solutions depending on heat treatment of the crystals. (A) $NaYF_4$:Ln $(HEDP)_{RT}$ nanocrystals, GRR = 0.037. (B) $NaYF_4$:Ln $(HEDP)_{320}$ nanocrystals, GRR = 0.154.

vacuum distillation of HEEDA is performed at 180 °C rather than 320 °C, for instance, the GRR value decreases to 0.109. Before the surface modification with HEDP, the purified particles display an even lower GRR value of only 0.045 (Figure 8). Similar values are observed for the respective colloidal solutions in water (Figure 9). In biolabeling applications either a very low or a very high GRR value is preferred because in these cases most of the light is emitted within a narrow spectral range.

Generally, a low GRR value is observed, if fast radiationless relaxation occurs from the green-emitting $^2H_{11/2}$ and $^4S_{3/2}$ levels to the red-emitting $^4F_{9/2}$ level. Fast depletion of the green-emitting levels can occur, for instance, by cross-relaxation between adjacent Er^{3+} ions and is observed in the bulk material if the Er^{3+} concentration is high.[23] Furthermore, any impurity in proximity to an Er^{3+} ion which increases the rate of multiphonon relaxation between these levels will decrease the GRR value of the material. In the bulk material, the presence of oxygen impurities in the fluoride lattice is believed to lower this rate.[23] Moreover, the GRR value is known to depend on the excitation density[16] and the crystallographic phase.[23,24] The GRR value of nanocrystals can be expected to be smaller compared to the bulk material since a large number of Er^{3+} ions should be located close to the surface and hence in proximity to defects, surface states, ligands, and impurities. In fact, the drastic increase of the up-conversion efficiency in the presence of HEDP at the surface is somewhat surprising because its phosphonate groups show strong IR bands at high frequencies (Figure 3) and should therefore be able to quench the excited Er^{3+} states. A likely explanation for the increased up-conversion efficiency is that HEDP replaces OH-groups or other small molecules at the particle surface which quench the excited Er^{3+} states more efficiently than HEDP. On the other hand, the low GRR values indicate that the radiationless recombination from the $^2H_{11/2}$ and $^4S_{3/2}$ levels to $^4F_{9/2}$ level remains high in the presence of HEDP. Whether the HEDP itself, other molecules at the particle surface, lattice defect in the interior of the nanocrystals, or the clustering of Er^{3+} ions is mainly responsible for the low GRR value of our nanocrystals is not yet clear. The successful synthesis of core−shell structures consisting of a $NaYF_4:Yb^{3+},Er^{3+}$ nanocrystal core and a pure $NaYF_4$ shell may help to distinguish between surface and bulk effects and may help to answer this question in the future.

Conclusion

By modifying the surface of $NaYF_4$:Yb,Er up-conversion nanocrystals with a diphosphonic acid, we have successfully prepared up-conversion nanocrystals which can be easily dispersed in water. Dynamic light scattering measurements prove that the particles are well-separated in aqueous solution. The surface modification increases the up-conversion efficiency significantly even in aqueous colloidal solution. The green-to-red ratio of the up-conversion emission is significantly lower compared to that of the bulk material, indicating fast radiationless depopulation of the green emitting energy level.

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