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Hydrothermal synthesis of poly(acrylic acid)-functionalized α-(β-)$NaYF_4$:Yb, Er up-conversion nano-/micro-phosphors

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ABSTRACT

Carboxylic acid-functionalized Yb^{3+}/Er^{3+} co-doped α- and β-$NaYF_4$ nano-/micro-spheres were prepared through a simple poly(acrylic acid) (PAA)-assisted hydrothermal process. Bovine serum albumin (BSA) protein was conjugated with Yb^{3+}/Er^{3+} co-doped α-(β-)$NaYF_4$ upconversion phosphors via free carboxylic acid groups on the surface of phosphors. The final products were characterized by X-ray diffraction (XRD), field emission scanning electron microscopy (FE-SEM), infrared (IR) spectrophotometer, ultraviolet (UV) spectrophotometer and photoluminescence spectroscopy (PL). XRD results showed that pure α-$NaYF_4$:Yb^{3+}, Er^{3+} nanospheres could be obtained via PAA assisted hydrothermal process at the pH value of 4–5 and 160 °C for 1–4 h. The obtained product is a mixture of α and β phases $NaYF_4$:Yb^{3+}, Er^{3+} when the reaction time increased from 5 to 24 h. When the solution was treated at 200 °C for 8–24 h at the pH value of 8–9, pure β-$NaYF_4$:Yb^{3+}, Er^{3+} microspheres were obtained. The FE-SEM results showed that the morphology of pure α-$NaYF_4$:Yb^{3+}, Er^{3+} was spherical nanoparticles with an average diameter of about 70 nm and the pure β-$NaYF_4$:Yb^{3+}, Er^{3+} was microsphere with an average diameter of about 700 nm, which is composed of spherical nanoparticles (30 nm). The FT-IR and UV spectra showed that BSA had been conjugated with α-$NaYF_4$:Yb^{3+}, Er^{3+} upconversion phosphors. The luminescence properties of α-(β-) $NaYF_4$:Yb^{3+}, Er^{3+} phosphors were also studied. Under 980 nm excitation, the upconversion luminescence (UCL) intensity of β-$NaYF_4$:Yb^{3+}, Er^{3+} microspheres was much stronger than that of α- $NaYF_4$:Yb^{3+}, Er^{3+} nanoparticles. Moreover, both red and green upconversion were ascribed to the two-photon process.

1. Introduction

Lanthanide (Ln) doped luminescence upconversion nanophosphors have attracted much attention in recent years owing to their wide applications in many fields, such as solid-state lasers [1], flat-panel displays [2], optical storage [3], photovoltaic cell [4], especially photothermal therapy [5,6], biological labels [7,8], bioimaging [9–14] and biomedicine [15–17]. Among the reported upconversion materials, Ln^{3+} doped $NaLnF_4$ phosphor due to the relatively low lattice phonon energy is considered to be one of the most efficient 980 nm NIR-to-visible upconversion fluorescent materials. To date, a lot of researches have focused on the study of preparation, luminescent properties of Ln^{3+} doped $NaYF_4$ and its biological applications including biological labels, multimodal bioimaging, photodynamic therapy, drug delivery, and small-animal imaging *in vivo* [5,18,19]. Recently, Qin's group [20] and Li's group [21,22] reported that lanthanide doped $NaLuF_4$ nanocrystals were more efficient than $NaYF_4$ nanocrystals. Due to a unique electronic state at the top of the valence band and smaller unit-cell volume, $NaLuF_4$ may be a more promising host for optical materials than $NaYF_4$ [23]. Compared with downconversion fluorescent materials, such as semiconductor quantum dots and organic dyes, upconversion nanophosphors have many obvious advantages including a weak autofluorescence background, high light-penetration depth in tissues, and minimum photodamage to living organisms [5]. Up to now, several approaches, such as high temperature thermal decomposition of trifluoroacetate precursors [24–26], hydro(solvo)thermal reaction [27–29], and ionic liquid-based synthesis [30,31] have been developed for the fabrication of rare earth-doped upconversion fluorescent $NaYF_4$ nanoparticles with different morphologies and unique luminescent properties. However, it is still a challenge to develop a simple technology for preparation rare earth co-doped α-(or β-) $NaYF_4$ nanophosphors with uniform shape, size, high luminescence, good biocompatible and solubility [18]. The upconversion nanophosphors should be water-soluble, and biocompatible, so that they can be easily conjugated with other targeted biomolecules when being applied in the field of biology [11]. Unfortunately, the rare earth ions doped $NaYF_4$ nanophosphors synthesized by above methods are unsatisfactory for using as biolabels directly because they have hydrophobic organic ligands with long hydrocarbon chains on the surface of nanophosphors,

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leading to low solubility in water and unfavorable surface properties [7]. Obviously, good solubility of upconversion nanophosphors in water is very important. To achieve this, different routes for the phase transfer of $NaYF_4$ hydrophobic nanophosphors from organic to aqueous phase via coated silica [15,32,33], ligand oxidation [7], coating with an amphiphilic polymer shell [25,34], and surface ligand exchange [35,36] have been reported. However, the above-mentioned phase transfer processes may be costly and complicated [7]. Therefore, it is a very necessary work for developing a simple one-step process to synthesize the upconversion nanophosphors with hydrophilic groups on the surface of the nanophosphors.

Poly(acrylic acid) (PAA) is a water-soluble anionic polymer which can coordinate with the surface of particle through functional groups of the polymer [25]. Several research groups have used PAA as a type of the polyelectrolyte molecules to replace the original hydrophobic ligands on the surface of metal oxides [35], semiconductor quantum-dot [37] and fluoride nanophosphors [35] via a ligand exchange procedure, and obtained highly monodisperse, good water-soluble nanophosphors for further conjugation with biomolecules. Wang et al. [38] reported the synthesis of PAA-functionalized cubic phase YF_3:Yb^{3+}/Er^{3+} upconversion luminescent nanocrystals with an average diameter of about 50 nm by one-pot hydrothermal process using PAA as a surfactant. Qin et al. [39] reported the preparation of water soluble cubic phase $NaYF_4$:Yb^{3+}, Tm^{3+} nanocrystals with an average size of ~40 nm by a facile solvothermal approach using polyvinylpyrrolidone (PVP) as a surfactant. Very recently, Li et al. [40] reported a new one-step synthetic strategy for high-quality surface-functionalized LaF_3:Yb^{3+}, Ho^{3+}/Tm^{3+} nanophosphors via a hydrothermal reaction assisted by binary cooperative ligands of hydrophilic 6-aminohexanoic and hydrophobic oleate ligands. However, to the best of our knowledge, there are no reports on the controlled synthesis of Yb^{3+}/Er^{3+} co-doped α-(β-)$NaYF_4$ upconversion nanophosphors by a simple hydrothermal process using PAA as a surfactant. In addition, it is well known that the upconversion luminescent efficiency of green emission in β-$NaYF_4$:Yb^{3+}, Er^{3+} is about 10 times stronger than that of α-$NaYF_4$:Yb^{3+}, Er^{3+} [41]. Therefore, how to obtain the pure, water-soluble cubic (α-) and hexagonal (β-) phase of $NaYF_4$:Yb^{3+}, Er^{3+} by using a simple one-pot hydrothermal process is a very significant work.

Taking into account the above reasons, in this work, we synthesized the Yb^{3+}/Er^{3+} co-doped α-(β-)$NaYF_4$ upconversion phosphors by a simple one-pot hydrothermal process using PAA as a surfactant. It is found that pH values, reaction temperature and time of hydrothermal treatment play important roles in the evolvement of crystalline phase and morphology of the final products. In addition, the BSA proteins were conjugated with Yb^{3+}/Er^{3+} co-doped α-$NaYF_4$ upconversion nanophosphors via free carboxylic acid groups on the surface of nanophosphors. The upconversion luminescence properties of products were also studied in details.

2. Experimental

2.1. Materials

All the chemical reagents used in this study were analytically pure grade without further purification. The rare earth oxides including Y_2O_3 (99.999%), Er_2O_3 (99.999%) and Yb_2O_3 (99.999%) were purchased from Shanghai Second Chemical Reagent Factory (China). Poly(acrylic acid) (PAA, $M_W = 1800$) was purchased from Aladdin Chemistry Co. Ltd. Coomassie Brilliant Blue G-250, NaOH, NaCl and ethanol were obtained from Tianjin Kermel Chemical Reagent (China). NH_4HF_2 was purchased from Sinopharm Chemical Reagent Co., Ltd (Shanghai, China). $Y(NO_3)_3 \cdot 6H_2O$, $Yb(NO_3)_3 \cdot 6H_2O$ and $Er(NO_3)_3 \cdot 6H_2O$ powders were obtained by dissolving the corresponding rare earth oxide in 6 mol/L of nitric acid and recrystallizing for four times. Bradford reagent was obtained by dissolving 100 mg of Coomassie Brilliant Blue G-250 in 50 mL of 95% ethanol, then adding 120 mL of 85% (w/v) phosphoric acid to this solution and diluting the mixture to 1 L with distilled water.

2.2. Preparation of α-$NaYF_4$:20%Yb^{3+}, 2%Er^{3+} nanoparticles

α-$NaYF_4$:20%Yb^{3+}, 2%Er^{3+} nanoparticles were synthesized as follows: NaCl (1.0 mmol), $Y(NO_3)_3 \cdot 6H_2O$ (0.78 mmol), $Yb(NO_3)_3 \cdot 6H_2O$ (0.20 mmol) and $Er(NO_3)_3 \cdot 6H_2O$ (0.02 mmol) were mixed with 10 mL distilled water in a 100 mL beaker under magnetic stirring until they were dissolved completely. A mixture of ethanol (30 mL) and 10 mL of PAA solution (5.0 wt.%) was dropped slowly in above rare earth nitrate solution. The solution was stirred for 10 min. Subsequently, 10 mL of NH_4HF_2 (2.0 mol/L) solution was added slowly to the above solution, and the pH value of solution was adjusted to 4–5 with 2 mol/L of NaOH under magnetic stirring at room temperature. After additional agitation for 20 minutes, the mixture solution was transferred to a 100 mL stainless Teflon-lined autoclave and heated at 160 °C for 4 h. As the autoclave was cooled to room-temperature naturally, the precipitates were separated by centrifugation, and washed with ethanol/water (v/v = 1:1) for four times. Finally, the α-$NaYF_4$:20%Yb^{3+}, 2%Er^{3+} nanoparticles were obtained after the precipitates were dried in air at 80 °C for 8 h.

2.3. Preparation of β-$NaYF_4$:20%Yb^{3+}, 2%Er^{3+} microspheres

A similar process was employed to prepare β-$NaYF_4$:20%Yb^{3+}, 2%Er^{3+}, except that the pH value of the final solution was adjusted to 8–9 by 2 mol/L of NaOH solution, and the mixed solution was hydrothermally treated at 200 °C for 8 h.

2.4. Bio-conjugation of BSA

BSA was linked to carboxyl groups existing on the surface of α-(β-)$NaYF_4$:20%Yb^{3+}, 2%Er^{3+} phosphors. First, the as-prepared upconversion phosphors were dissolved in 10.0 mL of DMF, then 0.20 mL of tri-*n*-butylamine and 0.10 mL of iso-butylchloroformate was added dropwise with stirring for 30 min. Iso-butylchloroformate is the leaving group and can react with esterified upconversion phosphors to form an active intermediate for further bioconjugation with BSA proteins. Finally, the BSA solution (0.2 g of BSA was dissolved in 4.0 mL de-ionized water and the pH value of solution was adjusted to 8–9 with 1 mol/L of NaOH aqueous solution under stirring in ice bath) was dropped slowly into the mixture under stirring at 4 °C. After 48 h, the products were centrifuged at 9000 r/min for 20 min and washed with de-ionized water for three times. The final products were dried in a vacuum freezing condition. The whole reaction and formation processes for the functionalization of α-$NaYF_4$:20%Yb^{3+}, 2%Er^{3+} upconversion nanophosphors with carboxyl groups (—COOH) and the subsequent conjugation with BSA on α-$NaYF_4$:20%Yb^{3+}, 2%Er^{3+} upconversion nanophosphors are described as follows (Scheme 1).

2.5. Characterization

The structure of all as-prepared products was characterized by X-ray powder diffraction (XRD), using a Japan Shimadzu XRD-6000 diffractometer with Cu K$\alpha 1$ radiation ($\lambda = 0.15406$ nm). The XRD data for index and cell parameter calculations were collected by a scanning mode with a step of 0.02° in the 2θ range from 10° to 60° and a canning rate of 2.0° min^{-1} with silicon used as an internal standard. FE-SEM images were obtained using a Hitachi S-4800 field emission scanning electron microscopy operating at acceleration voltage of 3 and 5 kV. Transmission electron microscopy (TEM) images were performed using a JEOL JEM-2100F with an acceleration voltage of 200 kV. An energy-dispersive X-ray analysis (EDX) of the samples was also performed during the TEM measurements. The UC emission spectra were taken on an F-4600 spectrophotometer equipped with an external tunable 4 W 980-nm laser diodes as the