CHEMISTRY
A EUROPEAN JOURNAL

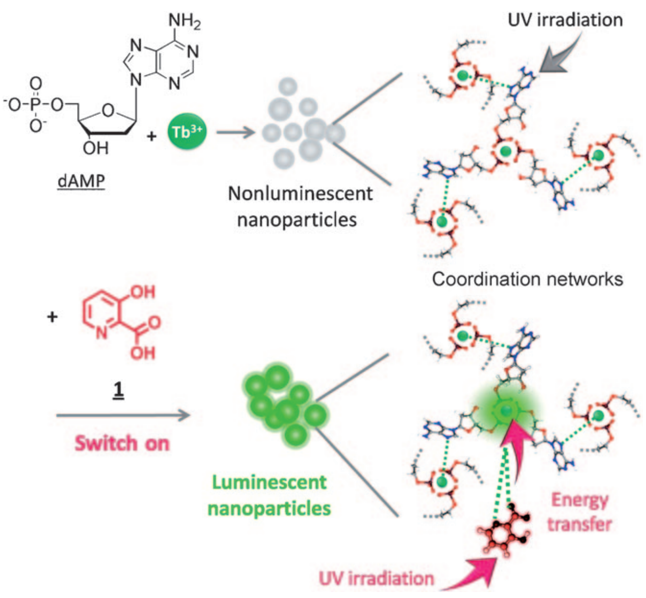
DOI: 10.1002/chem.201000007

Switching On Luminescence in Nucleotide/Lanthanide Coordination Nanoparticles via Synergistic Interactions with a Cofactor Ligand

Carole Aimé, Ryuhei Nishiyabu, Ryosuke Gondo, and Nobuo Kimizuka*[a]

Amorphous coordination nanoparticles (CNPs) formed from metal ions and synthetic ligand molecules have been emerging as a new family of functional nanomaterials.[1] They are made up of polymeric networks of ligands and metal ions[2] and have been applied in many fields including catalysis,[3] bioimaging[4] and drug delivery.[5] The majority of CNPs reported to date contain hydrophobic ligand molecules and consequently they have mostly been prepared in organic media. Meanwhile, we have recently reported that water-soluble nucleotides serve as bidentate ligands.[6] Upon mixing nucleotides and lanthanide ions in water, coordination networks consisting of phosphate, nucleobase units and lanthanide ions form spontaneously and give amorphous nanoparticle structures as determined by X-ray diffraction analysis.[6b] These nucleotide/lanthanide CNPs enjoy the full benefits of using biomolecules and lanthanide ions in water. For example, the large coordination number of lanthanide ions allows formation of amorphous coordination networks, in which densely accumulated nucleotides and lanthanide ions reveal efficient energy transfer and remarkable magnetic resonance imaging (MRI) properties.[6b] Moreover, they exhibit surprisingly adaptive self-assembly properties, that is, amorphous coordination networks are formed around a variety of water-soluble guest materials during the course of assembly.[6b,c] The design of adaptive self assembly is considered to be one of the forthcoming issues in supramolecular chemistry.[7]

We herein report a novel approach to bring out the latent photofunctionality of nucleotide/lanthanide complexes by inclusion of guest cofactor molecules. Synergistic interactions that operate between the cofactor ligands and host coordination networks confer the nucleotide/lanthanide CNPs signal-responsive characteristics. A combination of 2′-deoxyadenosine 5′-monophosphate (dAMP, Scheme 1) and terbium (Tb^{3+}) ions were selected for use in this study. We recently reported that CNPs consisting of guanine mononucleotides and Tb^{3+} ions show green luminescence upon photoexcitation of the guanine chromophore. This is ascribed to energy transfer from the guanine group to the emissive $^5D_4$ state of Tb^{3+} ion (antenna effect), which is secured by the coordination between two adjacent electron-density-rich atoms (O and N).[8] On the other hand, such a sensitization effect was highly specific for guanine-containing nucleotides and it was not observed for the other nucleotides. In the case of dAMP, the adenine nucleobase lacks the carbonyl group required for the coordination to lanthanide ions. The lower coordination ability of the adenine unit allows water



Scheme 1. Molecular structures of dAMP, hydroxypicolinic acid (**1**), and schematic representation of CNPs formed in the absence (top) and presence (bottom) of **1**.

---

[a] Dr. C. Aimé, Dr. R. Nishiyabu, R. Gondo, Prof. Dr. N. Kimizuka
Department of Chemistry and Biochemistry
Graduate School of Engineering, Kyushu University
JST, CREST, 744 Moto-oka, Nishi-ku, Fukuoka 819-0394 (Japan)
Fax: (+81) 92-802-2838
E-mail: n-kimi@mail.cstm.kyushu-u.ac.jp

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200100007.

molecules to compete for the coordination sphere of Tb^{3+}; this makes the complex increasingly nonradiative and significantly weakens its luminescence properties.

The disadvantage caused by employing an adenine nucleotide as one of the components, however, is surmountable by introducing guest cofactor molecules that coordinate to Tb^{3+} ions as ancillary ligands. Replacement of the coordinating water molecules by suitable cofactor ligands leads to conversion of the nonluminescent dAMP/Tb^{3+} complex into luminescent CNPs (Scheme 1). 3-Hydroxypicolinic acid (**1**, Scheme 1) was employed as a cofactor ligand because pyridine derivatives have been used as efficient sensitizers for lanthanide ions.[9]

Upon mixing dAMP and Tb^{3+} in water ([dAMP] = 0.75 mM, [Tb^{3+}] = 0.25 mM), colourless precipitates were formed that appeared as aggregated CNPs (average diameter ≈30 nm) in transmission electron microscopy (TEM, Figure 1 b) images. When the adenine chromophore in the resulting aqueous dispersion was photoexcited at 260 nm, emission from Tb^{3+} ions was not observed (sample 1 in Figure 1 a and Figure S1 in the Supporting Information). This confirms that energy transfer from the adenine base to Tb^{3+} does not occur in dAMP/Tb^{3+} CNPs.[6b] The ligand **1** was then introduced to the coordination sphere of the Tb^{3+} ion by adding aqueous $TbCl_3$ to the aqueous mixture of dAMP and **1** (denoted as (dAMP+**1**)/Tb^{3+}, dAMP/**1** = 15).

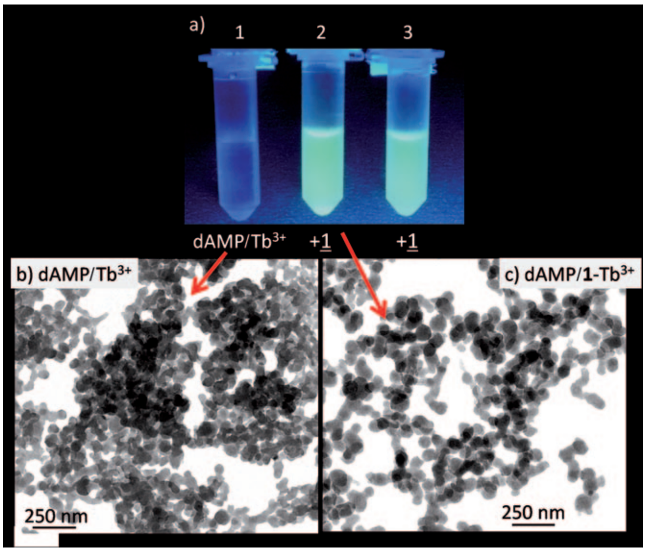


Figure 1. (a) Irradiation of CNPs formed upon mixing: (1) dAMP/Tb^{3+}, (2) (dAMP+**1**)/Tb^{3+}, (3) (dAMP/Tb^{3+}+**1**) using a UV lamp (λ_{ex} ≈365 nm). (b–c) TEM micrographs of dAMP/Tb^{3+} and (dAMP+**1**)/Tb^{3+} CNPs, respectively.

The free ligand **1** in water gives a strong $\pi\rightarrow\pi^*$ transition absorption maximum around 299 nm (Figure S2 in the Supporting Information). Mixing Tb^{3+} ions with aqueous **1** led to a small redshift of the $\pi\rightarrow\pi^*$ transition to 302 nm and appearance of a shoulder component around 338 nm (Figure S2 in the Supporting Information). This reflects complexation between **1** and Tb^{3+}, as will be discussed later. In the case of ternary aqueous mixture (dAMP+**1**)/Tb^{3+}, small shoulder components are noticeable around at 300 nm and 340 nm (Figure S4 in the Supporting Information). As dAMP and Tb^{3+} ions do not display absorption bands at these wavelengths, the shoulder components indicate coordination of **1** to Tb^{3+} ions in the aqueous mixture. Upon irradiation of the ternary aqueous mixture with a UV lamp (λ_{ex} ≈365 nm), bright green emission was observed by the naked eye (sample 2 in Figure 1 a). In the emission spectrum, luminescence peaks of the Tb^{3+} ion are observed at 489 ($^5D_4\rightarrow{}^7F_6$), 545 ($^5D_4\rightarrow{}^7F_5$), 586 ($^5D_4\rightarrow{}^7F_4$) and 621 nm ($^5D_4\rightarrow{}^7F_3$). Of these, the 545 nm band has the highest intensity (Figure 2 b, solid line). These observations indicate that the luminescence of Tb^{3+} is sensitized by **1** with high efficiency considering the low concentration of **1** employed (AMP/**1** = 15). The introduction of ligand **1** into the coordination networks did not affect the morphology of nanoparticles, as confirmed by TEM observation (Figure 1 c). The inclusion of guest molecules without impairing morphology of host assemblies is a key feature of adaptive self assembly. In the present case, coordination networks seem to flexibly rearrange themselves to follow the molecular shape of guest molecules.

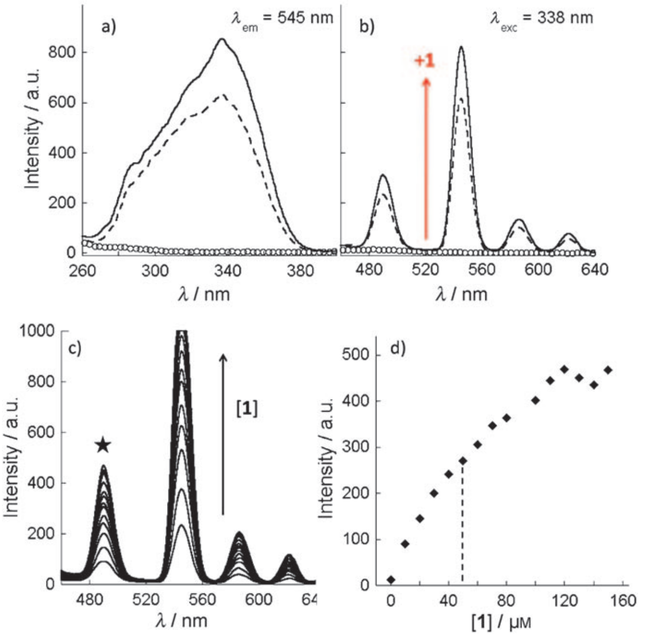


Figure 2. (a) Excitation and (b) emission spectra of (dAMP+**1**)/Tb^{3+} (solid line), (dAMP/Tb^{3+}+**1**) (dashed line), and dAMP/Tb^{3+} (open circles) ([**1**] = 50 μM). (c) Emission spectra of (dAMP+**1**)/Tb^{3+} with increasing concentration of **1** (10–160 μM), and (d) emission intensity evolution (λ_{em} = 489 nm, filled star Figure 2 c) as a function of [**1**] ([dAMP] = 0.75 mM, [Tb^{3+}] = 0.25 mM, λ_{em} = 545 nm, λ_{ex} = 338 nm).

Very interestingly, even when ligand **1** was successively added to an aqueous dispersion of preformed, nonluminescent dAMP/Tb^{3+} CNPs (dAMP/Tb^{3+}+**1**), it switched on the luminescence (sample 3 in Figure 1 a). When the excitation spectrum of this aqueous dispersion was monitored at $\lambda_{em} = 545$ nm, an intense peak was observed at 338 nm (Figure 2a, dashed line). This peak at 338 nm is distinct from the excitation peak of 300 nm observed for the aqueous solution of **1**/Tb^{3+} (without dAMP, Figure 3c, crosses and Figure S5 in the Supporting Information). It indicates that ligand **1** is bound to dAMP/Tb^{3+} CNPs, and photoexcitation of **1** caused energy transfer to the emissive $^5D_4$ state of Tb^{3+} ion; this resulted in the cofactor-sensitized luminescence (Figure 2b, dashed line). In the absence of **1**, naturally no excitation band was observed around 338 nm (open circles in Figure 2a). In Figure 2a and 2b the emission intensity at 545 nm is weaker for dAMP/Tb^{3+}+**1** (dashed line) compared to that observed for (dAMP+**1**)/Tb^{3+} (solid line). This suggests that, if successively added to aqueous CNPs of dAMP/Tb^{3+}, ligand **1** preferentially coordinates to Tb^{3+} ions present on the outer shell region of CNPs, because diffusion of **1** into the interior of CNPs could be limited by the existing dense coordination networks of dAMP/Tb^{3+}. We have recently reported that the coordination networks of nucleotide/lanthanide ions display barrier properties.[6c]

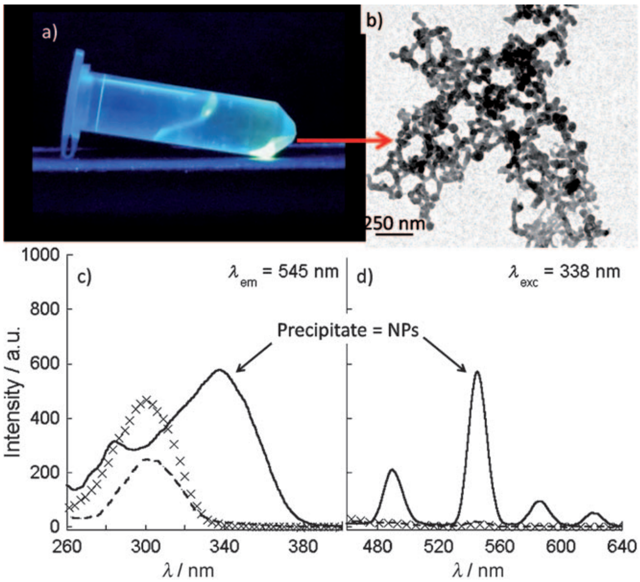


Figure 3. Luminescence properties of (dAMP+**1**)/Tb^{3+} CNPs in water: (a) irradiation of centrifuged specimen with a UV lamp ($\lambda_{ex} \approx 365$ nm), (b) TEM micrograph of the precipitate (c) Excitation and (d) emission spectra of (dAMP+**1**)/Tb^{3+} precipitate (solid line), and supernatant (dashed line). Luminescence and excitation spectra of **1**–Tb^{3+} in water (crosses) are also shown ([dAMP]=0.75 mM, [Tb^{3+}]=0.25 mM,[**1**]= 50 μM, $\lambda_{em} = 545$ nm, $\lambda_{ex} = 338$ nm).

Figure 2c and d show the dependence of Tb^{3+} luminescence intensity on the concentration of **1** in (dAMP+**1**)/Tb^{3+}. The emission intensity of Tb^{3+} increases with the concentration of **1**, whereas it levels off in cases in which the concentration of **1** reaches around 120 μM (Figure 2d). As the increase in Tb^{3+} luminescence intensity is conspicuous even at a concentration of **1** as low as 10 μM (AMP/**1**=75), the binding of **1** to dAMP/Tb^{3+} CNPs and concomitant photosensitization process appear to be efficient.

To gain more insight into the ternary complexation phenomena, the CNPs were separated from the bulk aqueous solution by using centrifugation. UV irradiation of the centrifuged specimen with a UV light showed strongly sensitized luminescence of Tb^{3+} from the precipitate but not from the supernatant (Figure 3a). TEM observations show that this luminescent fraction consists of aggregated CNPs (Figure 3b). The excitation spectra of the precipitated CNPs exhibited a maximum at 338 nm after removal of the supernatant and redispersion in ultrapure water. This peak is distinct from that observed for the supernatant fraction (excitation maximum at 300 nm, Figure 3c). As described previously, an excitation peak at 300 nm is typically observed for aqueous mixtures of **1** and Tb^{3+} (Figure 3c, crosses), and therefore the supernatant seems to contain the complex formed from these two components. On the other hand, an aqueous mixture of **1** and Tb^{3+} gave no aggregate structures by TEM, in contrast to dAMP/Tb^{3+}. This indicates that **1** does not serve as a bidentate ligand, which would be required for the formation of polymeric coordination networks. This supports that the luminescent CNPs observed in Figure 3b consist of ternary components, that is, dAMP, Tb^{3+} and ligand **1**.

It is interesting that the maximum intensities in excitation spectra of the precipitated CNPs (at 338 nm) and supernatant fraction (at 300 nm) are reached at considerably different wavelengths.[10] The observation of two excitation maxima indicates the presence of at least two coordination modes in the complex formed between **1** and Tb^{3+} in water and in aqueous dAMP/Tb^{3+} CNPs. The 3-hydroxypicolinate ligand **1** has been reported to form chelates that either have N,O-chelation (through the pyridine nitrogen and the carboxylate group, forming a five-membered chelate ring) or O,O-chelation (through the carboxylate group and the deprotonated hydroxyl group, forming a six-membered chelate ring).[9b] Figure S3 (Supporting Information) shows the pH dependence of absorption and excitation spectra obtained for aqueous mixtures of **1** and Tb^{3+}. Excitation spectra showed pH dependence that corresponds well to the dependence observed in absorption spectra. Upon increasing pH, absorption spectra showed a bathochromic shift from 300 nm (pH 4.4) to 338 nm (pH 7.4) with an isosbestic point. pK_a values for free **1** have been reported for the carboxylate group (<0), pyridine group (5.03), and hydroxyl group (11.06).[11a] The 300 nm absorption (pH 4.4) could then be ascribed to **1**/Tb^{3+} complexes with ligand **1** coordinating either in the zwitterionic form (N-protonated carboxylate) or in the monoanionic form (N-deprotonated carboxylate, N,O-chelation). The N,O chelation mode has been previously reported on the basis of X-ray crystal structures.[9b]

On the other hand, the absorption peak at 338 nm observed for **1**/Tb^{3+} (at pH 7.4) is considerably red-shifted compared with that observed for the dianionic free ligand **1** ($\lambda_{max} \approx 310$ nm, pH at ca. 11).[11b] Therefore, the 338 nm peak indicates that **1** is coordinated to Tb^{3+} ion, either in the anionic form (N,O-chelation) or in the dianionic form (O,O-chelation). The observed large spectral shift in the π→π* intraligand band might be ascribed to deprotonation of the phenolic group (O,O-chelation), because such a dramatic drop in the acid dissociation constant (pK_a) of a phenolic group has been observed for **1** upon coordination with trivalent metal ions.[11b] These observations indicate that the coordination mode of **1** is affected by the microenvironment of coordination networks provided by dAMP/Tb^{3+} CNPs. It indicates the existence of synergistic interactions operating between the cofactor ligand and the host coordination networks. We have reported that aqueous nucleotide/lanthanide CNPs will accommodate anionic guest molecules,[6b] and it is possible that anionic coordination form of ligand **1** is stabilized in CNPs. The cofactor ligand-induced switching of luminescence was also observed for the dCMP/Tb^{3+} nanoparticle system (Figure S6 in the Supporting Information), and this confirms the generality of the cofactor ligand-based photo-switching of CNPs.

In conclusion, we have demonstrated the use of 3-hydroxypicolinic acid (**1**) as an ancillary ligand to switch on the luminescence of nucleotide/lanthanide CNPs. Ligand **1** is easily incorporated into the coordination networks without impairing the nanoparticle structure. The formation of the ternary complex is reached either by mixing dAMP and **1** before addition of the Tb^{3+} ion [(dAMP+**1**)/Tb^{3+}] or by addition of **1** to preformed dAMP/Tb^{3+} CNPs (dAMP/Tb^{3+} +**1**). The coordination networks of nucleotides and lanthanide ions are capable of uptaking cofactor ligands, which coordinate to the Tb^{3+} centre probably by replacement of coordinating water molecules. The changes in the local coordination environment of Tb^{3+} ions consequently leads to the sensitized luminescence, in which the coordination mode is affected by synergistic interactions between **1** and the microenvironment provided by the CNPs. The doping of cofactor ligands provides a fundamental means to tune latent functionalities of CNPs, and this might open up new applications.

Acknowledgements

This work was financially supported by a Grant-in-Aid for the Global COE Program, "Science for Future Molecular Systems" from the Ministry of Education, Culture, Sports, Science and Technology of Japan, by Grant-in-Aid for Scientific Research (A) (No. 19205030) from Japan Society for the Promotion of Science, and by JST, CREST.

Keywords: coordination nanoparticles · lanthanides · luminescence · nucleotides · self-assembly

---

[1] a) W. Lin, W. J. Rieter, K. M. L. Taylor, *Angew. Chem.* **2009**, *121*, 660–668; *Angew. Chem. Int. Ed.* **2009**, *48*, 650–658; b) A. M. Spokoyny, D. Kim, A. Sumrein, C. A. Mirkin, *Chem. Soc. Rev.* **2009**, *38*, 1218–1227.

[2] a) M. Oh, C. A. Mirkin, *Nature* **2005**, *438*, 651–654; b) X. Sun, S. Dong, E. Wang, *J. Am. Chem. Soc.* **2005**, *127*, 13102–13103; c) M. Oh, C. A. Mirkin, *Angew. Chem.* **2006**, *118*, 5618–5620; *Angew. Chem. Int. Ed.* **2006**, *45*, 5492–5494; d) H. Maeda, M. Hasegawa, T. Hashimoto, T. Kakimoto, S. Nishio, T. Nakanishi, *J. Am. Chem. Soc.* **2006**, *128*, 10024–10025; e) I. Imaz, D. Maspoch, C. Rodriguez-Blanco, J. M. Perez-Falcon, J. Campo, D. Ruiz-Molina, *Angew. Chem.* **2008**, *120*, 1883–1886; *Angew. Chem. Int. Ed.* **2008**, *47*, 1857–1860; f) Y.-M. Jeon, G. S. Armatas, J. Heo, M. G. Kanatzidis, C. A. Mirkin, *Adv. Mater.* **2008**, *20*, 2105–2110; g) I. Imaz, J. Hernando, D. Ruiz-Molina, D. Maspoch, *Angew. Chem.* **2009**, *121*, 2361–2365; *Angew. Chem. Int. Ed.* **2009**, *48*, 2325–2329; h) Y. Geng, X.-J. Wang, B. Chen, H. Xue, Y.-P. Zhao, S. Lee, C.-H. Tung, L.-Z. Wu, *Chem. Eur. J.* **2009**, *15*, 5124–5129; i) Y.-M. Jeon, G. S. Armatas, D. Kim, M. G. Kanatzidis, C. A. Mirkin, *Small* **2009**, *5*, 46–50.

[3] K. H. Park, K. Jang, S. U. Son, D. A. Sweigart, *J. Am. Chem. Soc.* **2006**, *128*, 8740–8741.

[4] J. S. Kim, W. J. Rieter, K. M. L. Taylor, H. An, W. Lin, W. Lin, *J. Am. Chem. Soc.* **2007**, *129*, 8962–8963.

[5] W. J. Rieter, K. M. Pott, K. M. L. Taylor, W. Lin, *J. Am. Chem. Soc.* **2008**, *130*, 11584–11585.

[6] a) C. Aimé, R. Nishiyabu, R. Gondo, K. Kaneko, N. Kimizuka, *Chem. Commun.* **2008**, 6534–6536; b) R. Nishiyabu, N. Hashimoto, T. Cho, K. Watanabe, T. Yasunaga, A. Endo, K. Kaneko, T. Niidome, M. Murata, C. Adachi, Y. Katayama, M. Hashizume, N. Kimizuka, *J. Am. Chem. Soc.* **2009**, *131*, 2151–2158; c) R. Nishiyabu, C. Aimé, R. Gondo, T. Noguchi, N. Kimizuka, *Angew. Chem.* **2009**, *121*, 9629–9632; *Angew. Chem. Int. Ed.* **2009**, *48*, 9465–9468.

[7] a) J.-M. Lehn, *Chem. Soc. Rev.* **2007**, *36*, 151–160; b) O. Mamula, M. Lama, H. Stoeckli-Evans, S. Shova, *Angew. Chem.* **2006**, *118*, 5062–5066; *Angew. Chem. Int. Ed.* **2006**, *45*, 4940–4944; c) M. Schmittel, B. He, P. Mal, *Org. Lett.* **2008**, *10*, 2513–2516.

[8] a) P. K. L. Fu, C. Turro, *J. Am. Chem. Soc.* **1999**, *121*, 1–7; b) B. Lippert, *Coord. Chem. Rev.* **2000**, *200–202*, 487–516.

[9] a) K. O. Iwu, P. C. R. Soares-Santos, H. I. S. Nogueira, L. D. Carlos, T. Trindade, *J. Phys. Chem. C* **2009**, *113*, 7567–7573; b) P. C. R. Soares-Santos, H. I. S. Nogueira, V. Félix, M. G. B. Drew, R. A. S. Ferreira, L. D. Carlos, T. Trindade, *Chem. Mater.* **2003**, *15*, 100–108; c) W. J. Rieter, K. M. L. Taylor, W. Lin, *J. Am. Chem. Soc.* **2007**, *129*, 9852–9853; d) S. Comby, D. Imbert, A. S. Chauvin, J.-C. G. Bünzli, L. J. Charbonnière, R. F. Ziessel, *Inorg. Chem.* **2004**, *43*, 7369–7379; e) J.-C. G. Bünzli, L. J. Charbonnière, R. F. Ziessel, *J. Chem. Soc. Dalton Trans.* **2000**, 1917–1923; f) G.-L. Gu, R.-R. Tang, Y.-H. Zheng, X.-M. Shi, *Spectrochim. Acta Part A* **2008**, *71*, 209–214.

[10] Excitation of the supernatant at 300 nm lead to sensitized emission of Tb^{3+}, indicating the presence of molecular complexes **1**/Tb^{3+} (see the Supporting Information).

[11] a) A. K. W. Stephens, C. Orvig, *Inorg. Chim. Acta* **1998**, *273*, 47–53; b) M. Szabłowicz, E. Kita, *Transition Met. Chem.* **2004**, *29*, 762–768.

Received: January 4, 2010