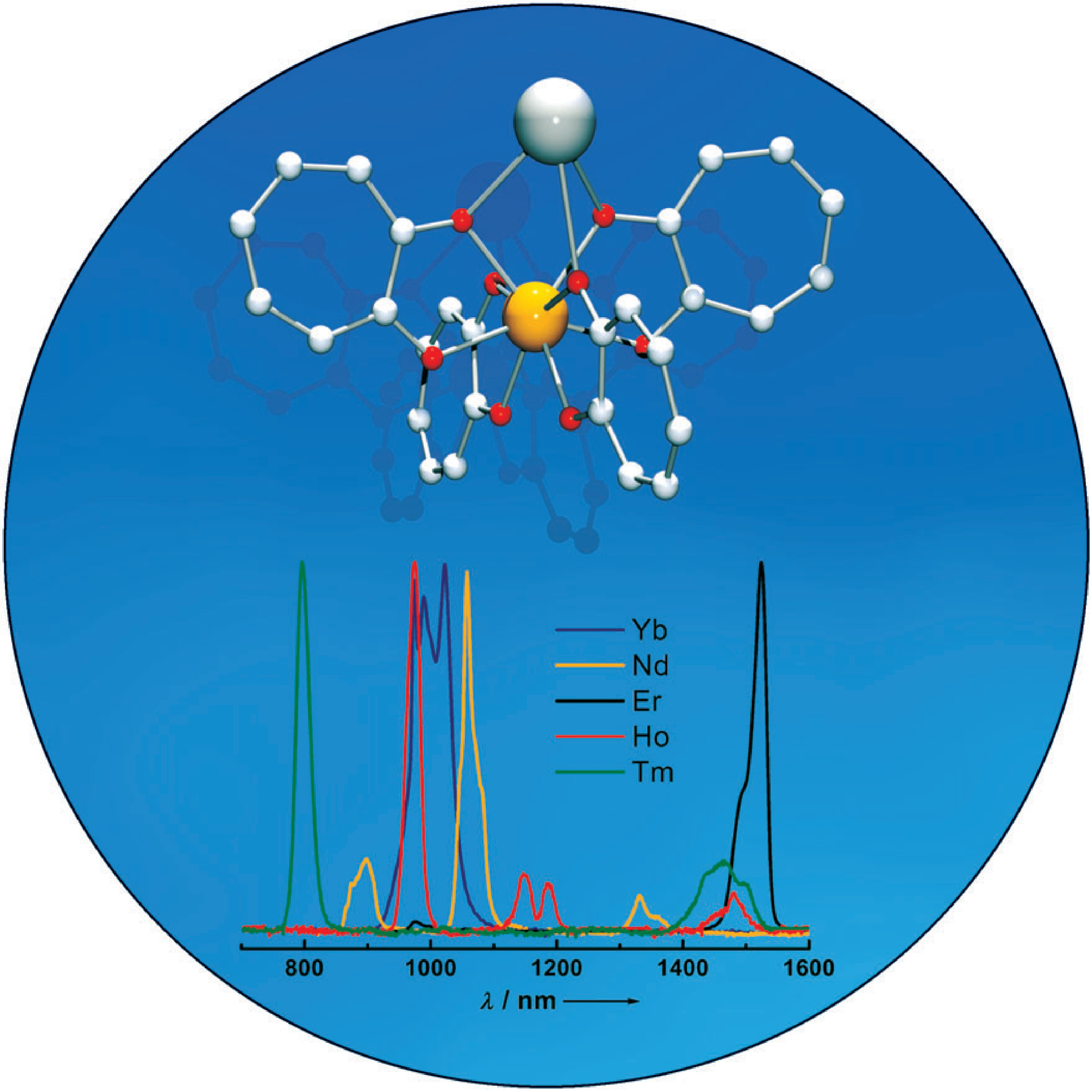
Zuschriften



Zweizähnige Tropolonat-Liganden sensibilisieren die Lumineszenz von Lanthanoid-Kationen, an die sie in Lösung unter Bildung von [Ln(tropolonat)$_4$]$^-$ koordinieren. Komplexe mit verschiedenen Ln-Ionen wurden strukturell charakterisiert. Weitere Informationen liefert die Zuschrift von S. Petoud und Mitarbeitern auf den folgenden Seiten.

DOI: 10.1002/ange.200463081

Luminescent Lanthanide Complexes

Sensitization of Near-Infrared-Emitting Lanthanide Cations in Solution by Tropolonate Ligands**

*Jian Zhang, Paul D. Badger, Steven J. Geib, and Stéphane Petoud**

The quest for luminescent reporters that emit in the near-infrared (NIR) domain is a target of prime importance, as NIR photons can penetrate deep into tissues without causing damage and without significant loss of intensity owing to the low absorption of NIR photons in such media.[1,2] Furthermore, the use of NIR light is one of the best strategies to obtain high-resolution pictures of deep tissues, as NIR light diffracts much less than visible light (diffraction is proportional to $1/(\lambda)^{SP}$, SP = scattering power).[3] NIR fluorescent organic dyes are the current candidates for such applications, but suffer from rapid photodecomposition when exposed to excitation light (photobleaching),[4] which prevents long exposure times or repetitive experiments and strongly limits the field of applications of these fluorophores. NIR luminescent lanthanide complexes are very promising reporters for detection in biological media for several reasons: 1) most lanthanide complexes do not photobleach,[5] 2) they display sharp emission bands that can be easily discriminated from background fluorescence,[6] and 3) they exhibit long luminescent lifetimes, which allow the removal of background fluorescence (autofluorescence) and increased assay sensitivity through time-resolved measurements.[7,8] Recent advances in technology allow such complexes to be excited in the NIR domain by using multiphoton excitation techniques.[9,10] So far, Nd and Yb complexes have been reported as NIR-luminescent reporters for these applications. However, there is still room for expanding the use of lanthanide complexes in biological applications. The molecules reported until now have limited luminescence output owing to low efficiency of intramolecular ligand-to-lanthanide energy transfer and/or insufficient protection of the metal ion against nonradiative deactivation processes. Furthermore, the sensitization of other lanthanide cations, such as Ho^{III} or Tm^{III}, is of high interest as supplementary emission wavelengths would then be also available. The narrow emission bandwidths of lanthanide cations allows for the simultaneous detection of several cations during the same experiment (multiplex assay). To obtain luminescent complexes for solution applications, the ligand(s) must harvest light and convert the resulting energy to the Ln^{III} ion (antenna effect),[11,12] as well as protect the Ln^{III} ion from nonradiative deactivations.[13] Oxygen-donor ligands that can efficiently absorb light are preferred because they also form strong bonds with lanthanide cations, which are hard Lewis acids.

We propose here a novel versatile approach to the development of lanthanide complexes that emit in the NIR based on tropolone as ligand. Upon deprotonation, tropolones (Figure 1) can be used as seven-membered ring, bidentate oxygen-donor chelators that allow direct coordination of the chromophoric group to the Ln^{III} cation. Their hard Lewis base character is suitable for forming strong bonds with Ln^{III}. Four tropolonate ligands are sufficient to complete the coordination number requirement of Ln^{III} (typically 8–12 in solution).[14,15] Tropolone has a good electronic structure to act as an antenna because the energy of its triplet state ($16800\ cm^{-1}$)[16] is compatible for efficient energy transfer to the low accepting levels of several Ln^{III} ions that emit in the NIR, such as Nd^{III}, Er^{III}, Ho^{III}, and Tm^{III}. For Yb^{III}, which has only one acceptor level ($^2F_{5/2}$) at $10200\ cm^{-1}$, the energy gap between the donor (ligand) triplet state and $^2F_{5/2}$ is quite large ($6600\ cm^{-1}$). Nonetheless, the phonon-assisted energy-transfer process could be used to explain the efficient energy transfer to Yb.[17] A large number of tropolone derivatives have been reported which allows for fine-tuning of the photophysical properties of the resulting lanthanide complexes. Herein we report the sensitization of several lanthanide cations that emit in the NIR (Nd^{III}, Er^{III}, Ho^{III}, Tm^{III}, and Yb^{III}) upon formation of the $[Ln(L)_4]^-$ complex ($L = C_7H_5O_2^-$; tropolonate) in aqueous and organic solutions.

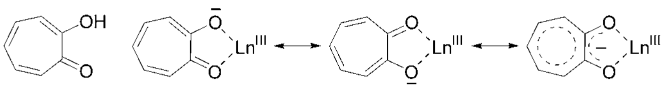


Figure 1. Structure of tropolone, and the coordination mode of tropolonate ligands with lanthanide (Ln^{III}) ions.

Muetterties and Wright previously identified that tropolonate ions can form both ML_3- and ML_4-type complexes depending on the experimental conditions.[18] They prepared ML_4 complexes by using NH_4^+ and Na^+ as the counterions, but crystal structures of the complexes were not reported. Upon changing the counterion to K^+, we were able to isolate and analyze the crystal structures of $\{K[Ln(L)_4]\cdot DMF\}_\infty$ (Ln = Tb, Dy, Ho, Er, Tm, Yb, Lu; DMF = *N*,*N*-dimethylformamide) for the first time. The Ln^{III} ion is coordinated by the eight oxygen atoms of four tropolonate ligands. The bridging K^+ counterion has a coordination number of seven through interactions with six oxygen atoms from two molecules of the complex and one oxygen atom from a solvent (DMF) molecule. The K^+ ion seems to play a significant role in the packing pattern of the complex in the crystal. The crystal structures of the complexes formed with Dy, Ho, Er, Tm, Yb, and Lu are isostructural (triclinic, $P\bar{1}$, $Z = 2$; see Figure 2) and differ from the structure of the Tb complex by the relative position of the K^+ ion with respect to the Ln^{III} ion. In all cases, the coordination polyhedron around the lanthanide cation is

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[*] J. Zhang, Dr. P. D. Badger, Prof. Dr. S. J. Geib, Prof. Dr. S. Petoud
Department of Chemistry
University of Pittsburgh
Pittsburgh, PA 15260 (USA)
Fax: (+1) 412-624-8611
E-mail: spetoud@pitt.edu

[**] The authors acknowledge financial support from the University of Pittsburgh.

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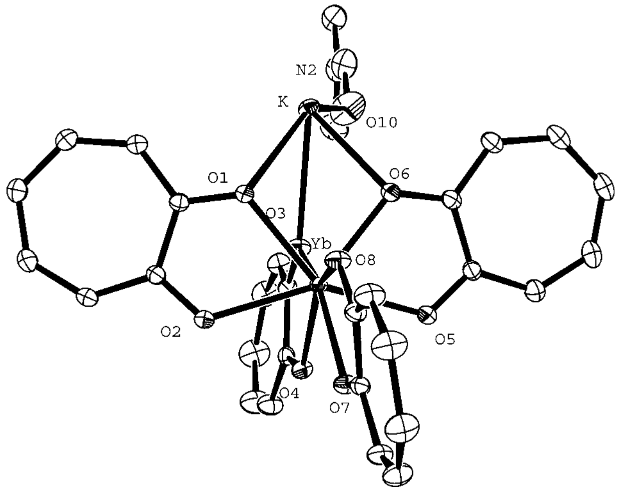

Figure 2. ORTEP drawing of K[Yb(L)$_4$]·DMF (50% probability level).

best described as a distorted dodecahedron (D_{2d}), one of the two most stable eight-coordinated polyhedra.

To confirm the stoichiometry of the complex in solution, an orientation spectrophotometric titration was performed by adding increasing amounts of Ln^{III} to a solution of the potassium salt of the tropolone ligand in DMSO. The absorption spectra recorded (see Supporting Information) reveal important changes upon addition of Ln^{III}. Preliminary treatment of these experimental data with SPECFIT software[19] indicates that four complexes are successively formed in solution (see Supporting Information); the calculated individual spectra of each of the four successive complexes ML$_1$, ML$_2$, ML$_3$, and ML$_4$ are uncorrelated.

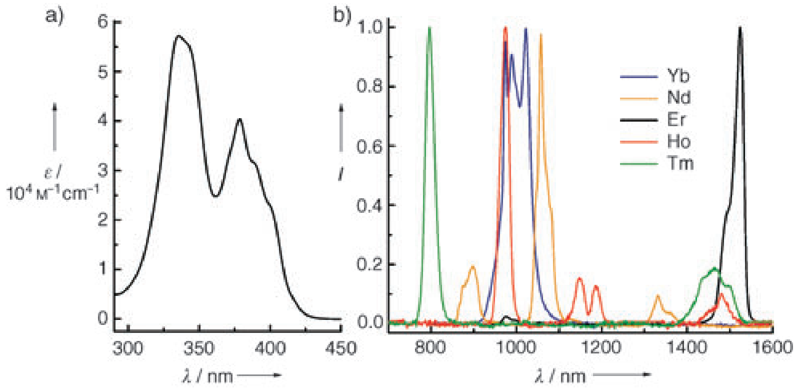

Figure 3. a) Absorption spectrum of [Yb(L)$_4$]$^-$ and b) normalized emission spectra of [Ln(L)$_4$]$^-$ with Ln = Yb, Nd, Er, Ho, and Tm (10^{-5} M in dimethylsulfoxide (DMSO)) in the NIR at 298 K upon ligand excitation at 340 nm using a Xenon lamp as excitation source.[20]

Upon formation of the corresponding ML$_4$ complexes, several lanthanide cations could be sensitized through the tropolonate ligands (Figure 3). Corresponding with ligand-to-metal energy transfer, the intensity of the fluorescence decreased for the tropolonate ligand which is centered in the visible region at 425 nm, while the luminescence of the corresponding lanthanide ion appeared as sharp emission lines in the NIR range. For the Nd complex, emission bands were observed at 897, 1056, and 1331 nm and are attributed to the ${}^4F_{3/2}\rightarrow{}^4I_{9/2}$, ${}^4F_{3/2}\rightarrow{}^4I_{11/2}$, and ${}^4F_{3/2}\rightarrow{}^4I_{13/2}$ transitions, respectively. For the Yb complex, there is only one emission band affected by crystal-field splitting which is assigned to the ${}^2F_{5/2}\rightarrow{}^2F_{7/2}$ transition. An observed emission band at 1524 nm is attributed to the ${}^4I_{13/2}\rightarrow{}^4I_{15/2}$ transition for Er. To the best of our knowledge, the emission of a holmium complex in solution is reported here for the first time: Four emission bands were observed. The emission bands at 975 and 1479 nm are assigned to ${}^5F_5\rightarrow{}^5I_7$ and ${}^5F_5\rightarrow{}^5I_6$ transitions, respectively. The emission bands at 1148 and 1187 nm are assigned to the same ${}^5I_6\rightarrow{}^5I_8$ transition split into two components. The emission bands of the Tm complex observed at 796 and 1465 nm are assigned to ${}^3F_4\rightarrow{}^3H_6$ and ${}^3F_4\rightarrow{}^3H_4$ transitions, respectively. The ligand-centered emission does not completely disappear when the lanthanide cation is added in any of these cases which indicates that the ligand-to-lanthanide energy-transfer process is not complete and that further optimization is possible.

The fact that the tropolonate ion can sensitize not only Yb, Nd, and Er but also Ho and Tm indicates that it is a very promising and versatile sensitizer for lanthanide cations that have acceptor levels located at relatively low energies. The narrow emission bands of lanthanide cations allow the simultaneous detection of several lanthanide cations during the same experiment by using a single excitation wavelength—a useful feature for multiplex assays.

To quantify the intramolecular ligand-to-lanthanide energy transfer as well as quenching processes that take place in the different lanthanide complexes, luminescence quantum yields upon ligand excitation were measured in various solvents (Table 1). Quantum yield values reported for the Yb^{III} complex compare well to those reported for other Yb^{III} complexes and are among the highest values.[21] There is a significant difference between measurements made in deuterated and non-deuterated solvents which indicates the presence of a nonradiative deactivation process. This dependency on the nature of the solvent suggests that the Ln^{III} cations are not completely protected from the solvent by the four tropolone ligands in solution. Nevertheless, the ligand-to-lanthanide energy-transfer process and the protection offered by the coordinated

Table 1: Absolute emission quantum yields (Φ) for [Ln(L)$_4$]$^-$ in organic and aqueous media.[a]

Ln	Solvent	Φ_{Ln}	Φ_{Ln} (deuterated solvent)
Yb	DMSO	$1.9\pm0.1\times10^{-2}$	$2.2\pm0.3\times10^{-2}$
Yb	MeOH	$1.3\pm0.2\times10^{-3}$	$1.6\pm0.2\times10^{-2}$
Yb	H_2O	$2.4\pm0.3\times10^{-4}$	$7.4\pm0.1\times10^{-3}$
Nd[b]	DMSO	$2.1\pm0.1\times10^{-3}$	$3.6\pm0.7\times10^{-3}$
Er[b]	DMSO	$1.7\pm0.1\times10^{-4}$	$3.2\pm0.4\times10^{-4}$
Tm[c]	DMSO	$3.8\pm0.2\times10^{-5}$	$5.7\pm0.2\times10^{-5}$
Ho[c]	DMSO	$2.3\pm0.2\times10^{-5}$	$2.4\pm0.1\times10^{-5}$

[a] λ_{ex} = 340 nm was used for quantum yield determinations. [b] Quantum yields were measured using [Yb(L)$_4$]$^-$ as standard. [c] Quantum yields were measured using [Er(L)$_4$]$^-$ as standard.

ligands are sufficient to allow the measurement of the quantum yields of the Yb complex in water. The quantum yield values recorded for $[Ln(L)_4]^-$ with Ln = Nd, Er, Ho, and Tm are lower than those recorded with Ln = Yb, but are still easily measurable with a fluorimeter using a Xenon lamp as a source of excitation.

By using the formula established by Beeby et al.[13] and on the basis of the lifetimes (τ) of the Yb^{III} complexes recorded in H_2O and D_2O ($\tau_{H2O} = 0.75 \pm 0.01$ µs, $\tau_{D2O} = 10.03 \pm 0.11$ µs), we found that 1.1 molecules of water are directly bound to the lanthanide cation when the complex is in solution. The same result was obtained when the lifetimes measured in MeOH and CD_3OD ($\tau_{CH3OH} = 1.62 \pm 0.03$ µs, $\tau_{CD3OD} = 13.02 \pm 0.01$ µs) were used. This observation indicates that the structures observed in the solid state, in which no solvent molecules are bound to the lanthanide cation, are different from the structures of the lanthanide complexes in solution. The presence of nonradiative processes partially explains the low quantum yields observed for tropolonate complexes in water.

In conclusion, we have identified the structure of ML_4 complexes formed between bidentate tropolonate ligands and seven different lanthanide cations: Tb^{III}, Dy^{III}, Ho^{III}, Er^{III}, Tm^{III}, Yb^{III}, and Lu^{III}. The coordination geometry around the lanthanide cations is close to a dodecahedron. The intermolecular packing patterns are different between the Tb complex and the complexes formed with the other lanthanide cations reported here. Quantitative luminescence measurements indicated that tropolonate ligands are able to sensitize several lanthanide cations that emit in the near-infrared domain. Also, the luminescence of Ho^{III} in a lanthanide complex in solution is reported here for the first time. Quantum yields of the complexes formed with Yb^{III} are comparable to the highest reported quantum yields of other lanthanide complexes that emit in the NIR domain in organic solvents. In aqueous solution, water has a very strong deactivating effect on the luminescence of lanthanide ions owing to the coordination to Ln^{III} of water molecules, which were not present in the solid state.

Owing to the flexibility of the approach, limitations can be removed by preparing a multidentate ligand that connects several chelating tropolone units to a common backbone. The backbone will function 1) to improve protection of the lanthanide cation from nonradiative deactivation by preventing the access of water molecules to the metal ion and 2) to increase the stability of the complex in solution, a useful feature when the complex is used at low concentrations. Emission spectra of the complexes indicate that for all the studied lanthanide complexes here, there is a significant amount of residual ligand emission. This is an indication of incomplete energy transfer from the ligand to the lanthanide ion. The preparation of derivatives of tropolone ligands is underway to optimize this parameter.

Experimental Section

Tropolone, $LnCl_3 \cdot n H_2O$ (99.99 %), and methanolic KOH (0.103 M) were purchased from Aldrich. The complexes were synthesized as follows: KOH (0.04 mmol) in methanol was added to a solution of tropolone (0.04 mmol) in methanol (10 mL). $LnCl_3 \cdot n H_2O$ (Ln = La, Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, and Lu; 0.01 mmol) in methanol (10 mL) was then added to the resulting solution. The precipitate was filtered, washed three times with methanol, and dried in vacuo over P_2O_5 for 48 h. Elemental analysis: calcd for $C_{28}H_{20}O_8KYb$ (%): C 48.28, H 2.89; found: C 48.47, H 2.92; ESI-MS: m/z: 736 $[M+K]^+$, 576 $[M-L]^+$, 416 $[M-2L-K]^+$. Single crystals of $\{K[Ln(L)_4]\cdot DMF\}_\infty$ were obtained by slow diffusion of diethyl ether into concentrated solutions of $[Ln(L)_4]^-$ in DMF.

Crystal data for $\{K[Yb(L)_4]\cdot DMF\}_\infty$: $C_{31}H_{27}KNO_9Yb$, $M = 769.68$, triclinic, $P\bar{1}$, $a = 7.2409(3)$, $b = 10.9079(4)$, $c = 19.8683(7)$ Å, $\alpha = 80.0870(10)$, $\beta = 84.1570(10)$, $\gamma = 78.8690(10)°$, $V = 1512.93(10)$ Å^3, $T = 298$ K, $Z = 2$, $\lambda Mo_{K\alpha} = 0.71073$ Å, 19668 reflections measured of which 10293 were unique ($R_{int} = 0.014$), 10027 observed reflections $[I > 2\sigma(I)]$ were used in all calculations, $R(F) = 0.0209$, $R_w = 0.0544$. Crystal data for $\{K[Tb(L)_4]\cdot DMF\}_\infty$: $C_{31}H_{27}KNO_9Tb$, $M = 755.56$, monoclinic, $P2_1/n$, $a = 12.7566(12)$, $b = 13.2771(12)$, $c = 18.9393(18)$ Å, $\beta = 95.984(2)°$, $V = 3190.3(5)$ Å^3, $T = 298$ K, $Z = 4$, $\lambda Mo_{K\alpha} = 0.71073$ Å, 40368 reflections measured of which 11227 were unique ($R_{int} = 0.0588$), 6647 observed reflections $[I > 2\sigma(I)]$ were used in all calculations, $R(F) = 0.0521$, $R_w = 0.1017$. CCDC 252899 ($\{K[Yb(L)_4]\cdot DMF\}_\infty$), 252900 ($\{K[Tb(L)_4]\cdot DMF\}_\infty$), 252901 ($\{K[Dy(L)_4]\cdot DMF\}_\infty$), 252902 ($\{K[Ho(L)_4]\cdot DMF\}_\infty$), 252903 ($\{K[Er(L)_4]\cdot DMF\}_\infty$), 252904 ($\{K[Tm(L)_4]\cdot DMF\}_\infty$), and 252905 ($\{K[Lu(L)_4]\cdot DMF\}_\infty$) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

FT-IR spectra were obtained from samples prepared as KBr pellets on a Perkin–Elmer BX spectrometer. Absorption spectra were recorded on a Perkin–Elmer Lambda 9 spectrophotometer coupled with a personal computer and by using software supplied by Perkin–Elmer. Emission and excitation (lanthanide luminescence) spectra were measured using a Jobin Yvon–Horiba Fluorolog-322 spectrofluorimeter equipped for measurements at both RT and 77 K (Hamamatsu R928 detector for the visible domain; DSS-IGA020L (Electro-Optical Systems, Inc.) detector for the NIR domain). Luminescence and excitation spectra were corrected for the instrumental function. Yb^{III} luminescence quantum yields were measured by using the
$^4G_{5/2} \rightarrow {}^6H_{9/2}$ transition of a previously reported samarium–(2-hydroxyisophthalamide) macrobicyclic complex ($\Phi = 7.3 \times 10^{-4}$ in 0.01 M TRIS buffer) as reference.[15] For convenience, the Yb complex was used as the standard for the quantum yield measurements of the Nd and Er complexes. The quantum yields for Tm and Ho complexes were measured by using the Er complex as the standard for better accuracy because of their comparable luminescence intensities. Detailed experimental setup and methods for photophysical measurements are described in the Supporting Information. Crystals for diffraction studies were attached to glass fibers with epoxy cement. X-ray data were collected on a Bruker Smart Apex CCD diffractometer by using graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). Data processing, and structure solution and refinements were performed with the Bruker Smart, Saint, and SHELXTL program packages, respectively. All structures were solved by direct methods. All non-hydrogen atoms were refined anisotropically.

Received: December 28, 2004

Keywords: lanthanides · luminescence · near-infrared emitters · O ligands · sensitizers

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