‖ **Lanthanides** │*Hot Paper*│

One-Step Assembly of Visible and Near-Infrared Emitting Metallacrown Dimers Using a Bifunctional Linker

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Abstract: A family of dimeric $Ln^{III}[12-MC_{Ga(III)N(shi)}-4]$ metallacrowns (MCs) (Ln^{III} = Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, and Yb) was synthesized using the isophthalate group (ip^{2-}) as a linker. The $[LnGa_4]_2$ complexes exhibit remarkable photophysical properties, with large molar absorptivities of $\approx 4 \times 10^4$ M^{-1} cm^{-1}, high quantum yields and long luminescence lifetimes with values of (i) 31.2(2)% and 1.410(1) ms, respectively for the visible-emitting $[TbGa_4]_2$ complex and (ii) 2.43(6)% and 30.5(1) μs for the near-infrared (NIR) emitting $[YbGa_4]_2$ in the solid state. The NIR emission was obtained not only from Yb, Nd, and Er complexes but also from the less frequently observed emitters such as Pr and Ho. In addition, emission in both visible and NIR domains could be detected for Dy and Sm MCs. ESI-MS and UV/Vis data revealed that the complexes are highly stable in dimethylsulfoxide (DMSO) solution with the ^{1}H- and COSY-NMR spectra of the diamagnetic $[YGa_4]_2$ analogue providing evidence for long-term solution stability. This new approach allows one to construct a basis for highly luminescent MCs that may be further modified to be adapted for applications such as optical imaging.

Metallacrowns (MCs) are a unique class of inorganic macrocycles forming repeating [Metal-N-O] subunits with a large variety of structures of different sizes and topologies being synthesized in the last two decades.[1] These MC complexes typically use tetradentate hydroximate types of ligands such as salicylhydroximate (shi^{3-}) (Figure 1) with oxygen atoms oriented toward the center of the ring allowing an efficient pre-organi-

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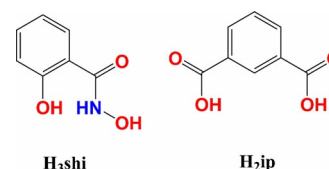
Figure 1. Structures of salicylhydroxamic acid (H₃shi) (left) and isophthalic acid (H₂ip) (right).

zation for guest encapsulation in a manner similar to classical organic crown ethers. Accordingly, MCs coordinate a central metal cation through these oxygen binding sites and provide an appealing route toward the a priori design of multimetallic complexes. Recently, lanthanide (Ln^{III})-encapsulated MCs have drawn strong interest due to their remarkable luminescent properties in the near-infrared (NIR) range, with the highest quantum yield values reported to date for Nd^{III} and Yb^{III} complexes containing C−H bonds.[2] In addition, the MC approach has led to families of complexes displaying luminescent sensitization of multiple lanthanide ions in both visible and NIR regions,[2c] a feature that has been described only for a few systems.[3] Very recently, we have reported the first direct applications of NIR-emitting MCs for the selective imaging of necrotic cells versus apoptotic or healthy cells, or as simultaneous cell fixation and counter-staining agents.[4]

For many applications such as optical imaging, the total number of emitted photons is crucial for detection sensitivity. Since most of the f–f transitions are forbidden, free lanthanide cations have very low absorption cross sections and need to be sensitized by highly absorbing chromophoric groups that will transfer the resulting energy to the accepting electronic levels of the Ln^{III}. This process is named "antenna effect"[5] and has a high impact on the total number of emitted photons. A major advantage of Ln^{III}-based MC imaging agents is that they can be constituted with chromophoric aromatic ligands connected to several diamagnetic metal ions creating a rigid tridimensional structure with large absorptivity. This assembly allows to establish a controlled, constant and relatively long distance between the Ln^{III} and the O−H, N−H, or C−H oscillators located on these chromophoric ligands. Such organization is advantageous as overtones of these vibrations can quench significantly Ln^{III} emission if the distance between the two partners is very short.[6] In addition, MCs incorporate a large number of chromophoric ligands, increasing the absorption of each discrete MC molecule, and in turn the number of emitted photons. All mentioned features of the MC structure should

contribute to the increase of the overall luminescence intensity and brightness of the complexes.

One particularly promising class of MCs previously reported by our group,[2c] Ln^{III}(benzoate)$_4$[12-MC$_{Ga(III)N(shi)}$-4] (hereafter LnGa$_4$), are assembled by the reaction between salicylhydroxamic acid (H$_3$shi) with sodium benzoate, pyridine, gallium (Ga) and lanthanide nitrates to form a series of LnGa$_4$ complexes. These MCs are attractive precursors for higher nuclearity MCs because of the presence of four benzoate ligands on the same side of the Ga$_4$ plane (Figure 2, top left), which could favor the
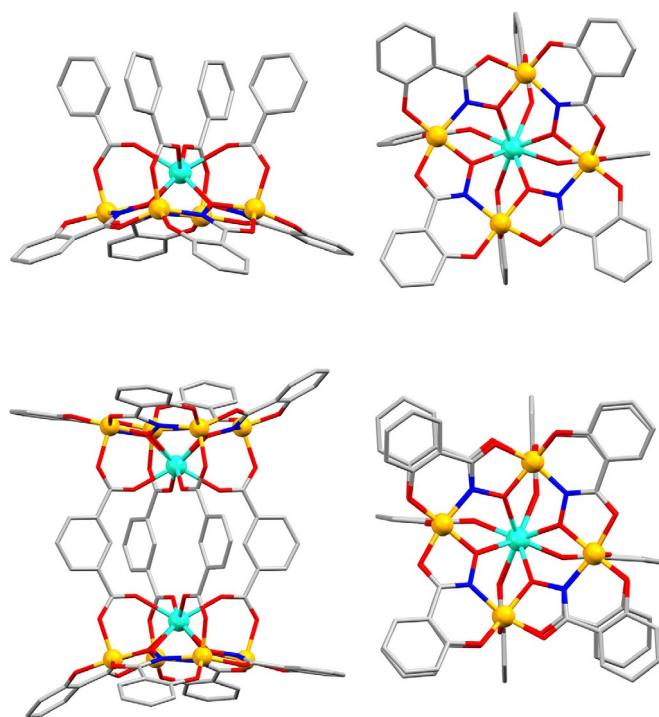

Figure 2. Structures of DyGa$_4$ MC (top) and [DyGa$_4$]$_2$ dimeric complexes (bottom) obtained from X-ray diffraction on single crystals: (left) side-view and (right) top-down view of the 12-MC-4 core. Color code: Ga, yellow; Dy, teal; O, red; N, blue; C, grey. Solvents, counter cations, and hydrogen atoms have been omitted for clarity.

formation of discrete assemblies when *meta*-directed dicarboxylate ligands are used instead of benzoate ligands. The functionalization of emissive molecules in order to target specific biological entities such as tumors or cellular elements or to add additional detection modalities is an objective in high demand. The decoration of the backbone ligand with a second type of functionality is challenging due to the self-assembly process controlling the formation of the MC complex. The introduction of a second site with these *meta*-directed "bridging" ligands, should ideally enhance the thermodynamic stability and/or kinetic inertness in comparison to the corresponding MCs formed with benzoate, and could serve as a tether to provide the desired diversity to enhance a well-controlled MC cell targeting.

Herein, we report the synthesis and characterizations of a family of highly stable self-assembled molecules that are dimers of the corresponding LnGa$_4$ MCs (Ln = Pr, Nd, Sm, Eu,

Gd, Tb, Dy, Ho, Er, Tm, and Yb). These complexes retain the luminescence properties of LnGa$_4$ MCs across the entire Ln series, while providing an enhanced solution stability and a possibility for functionalization by varying the nature of the binding ligand. Furthermore, by doubling the number of antenna ligands, [LnGa$_4$]$_2$ may offer a superior luminescence intensity and brightness.

A consideration of the directional bonding approach from the supramolecular chemistry field[7] led to the selection of the isophthalate (ip^{2-}) group as the linker for these MCs. The reaction of H$_3$shi, isophthalic acid, Ga(NO$_3$)$_3$, and Ln(NO$_3$)$_3$ in a 8:4:8:2 molar ratio in presence of an excess of NH$_4$HCO$_3$ in DMF gave a clear solution, which was left for slow evaporation. After two weeks, crystals of [Ga$_8$Ln$_2$(shi)$_8$(ip)$_4$(DMF)$_2$(H$_2$O)$_2$]-(NH$_4^+$)$_2$·xDMF·yH$_2$O ([LnGa$_4$]$_2$) grew in 10–35% yields.

The [LnGa$_4$]$_2$ complexes crystallize in the monoclinic space group $P2_1/n$ and form a dimer of [LnGa$_4$] subunits bridged by four ip^{2-} ligands (Figure 2, bottom left showing for [DyGa$_4$]$_2$). Although the two [DyGa$_4$] subunits are crystallographically inequivalent, their structures are essentially similar and resemble the structure of the parent DyGa$_4$ MC (Figure 2), in which the 12-MC-4 core contains four Ga^{III} ions linked by four shi^{3-} ligands in a nearly planar geometry. The central Dy^{III} ion is bridged to the Ga^{III} ring by four carboxylate ligands and adopts an 8-coordinate square-antiprism geometry.[2c] The four rigid ip^{2-} ligands lock the two Dy^{III} cations at a fixed distance of 7.224(1) Å. The chemical formula of [LnGa$_4$]$_2$ complexes were further confirmed by ESI-MS and elemental analysis studies (Supporting Information).

It is worth noting that similar [LnGa$_4$]$_2$ complexes were also obtained by performing a carboxylate substitution on the LnGa$_4$ MCs with isophthalic acid.

From the ESI-MS studies, the [LnGa$_4$]$_2$ complexes were found to be highly soluble and stable in DMSO. UV/Vis absorption spectra of a representative complex, [TbGa$_4$]$_2$, were collected in a DMSO solution and the absorbance intensity was monitored over a period of 24 hours (Figure S2). The complex exhibits absorption bands in the range of 200–350 nm with a low-energy maximum located around 310 nm ($\varepsilon \approx 4 \times 10^4$ M^{-1} cm^{-1}). This band is redshifted by 10 nm in respect to the backbone ligand alone (H$_3$shi). A similar effect was observed upon formation of LnGa$_4$ MCs previously reported.[2c] The value of the molar absorption coefficient of [LnGa$_4$]$_2$, mainly due to $\pi^* \leftarrow \pi$ transitions (on the basis of the extinction coefficient) associated with the presence of eight aromatic shi^{3-} ligands, is about twice the value measured for LnGa$_4$ MCs.[2c] The absorbance value corresponding to these bands does not significantly change during the 24 hour measurement, confirming a good level of stability of the complex in DMSO solution.

The diamagnetic [YGa$_4$]$_2$ analog was also isolated and subjected to NMR analysis. The NMR peaks were assigned as shown in Figure 3 (top), which agree with the ratio 2:1 of shi^{3-}:ip^{2-} on the complex. Peaks for H$_e$ and H$_f$ protons are split into two groups of peaks, probably due to the non-equivalence between the two [YGa$_4$] subunits observed in the X-ray structure. The peak assignment was confirmed by the ^{1}H–^{1}H COSY-NMR spectrum Figure 3 (bottom), which allows the de-

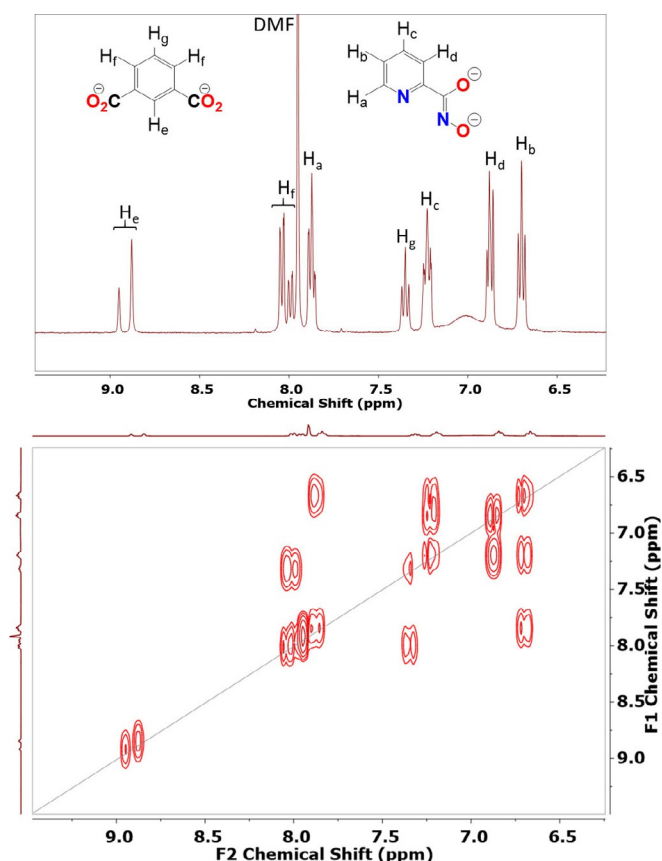**Figure 3.** (Top) ^1H NMR spectrum and (Bottom) ^1H–^1H COSY-NMR spectrum of the complex [YGa$_4$]$_2$ obtained in [D$_6$]DMSO.

termination of neighboring protons exhibiting correlations due to spin-spin coupling. Identical NMR spectra were obtained after one week, which confirms the long-term solution stability of these [LnGa$_4$]$_2$ complexes.

In the solid state, diffuse reflectance spectra of [LnGa$_4$]$_2$ complexes, presented as Kubelka–Munk functions, show broad ligand-centered bands in the range 250–350 nm with additional sharp features of much lower intensity which can be assigned to f–f transitions of Pr, Nd, Sm, Ho, Er and Tm ions (Figure S2). As in the case of the EuGa$_4$ MC,[2c] the diffuse reflectance spectrum of the Eu^{III} analogue of [LnGa$_4$]$_2$ demonstrates a broadening when moving towards longer wavelengths up to

450 nm, due to the presence of ligand-to-metal charge transfer (LMCT) states. Depending on the level of their energy, such electronic states can either quench or sensitize Eu^{III} emission.[8a]

Excitation spectra (Figure S4) of the MCs formed with the different Ln^{III} upon monitoring the main f–f transitions in the visible or NIR ranges show the presence of a series of broad bands located in the same energy range as the ones of the corresponding diffuse reflectance spectra (Figure S2). These observations indicate that the MC scaffold in [LnGa$_4$]$_2$ can sensitize different Ln^{III} cations through an antenna effect. The sharper bands present in the excitation spectra of [LnGa$_4$]$_2$ can be attributed to the f–f transitions and reflect the possibility of direct excitation of most of the studied Ln^{III}. The energy position of the triplet state (T$_1$) determined as a 0–0 band from the phosphorescence spectrum of the [GdGa$_4$]$_2$ complex in the solid state (Figure S3) is located around 21 980 cm^{-1} (455 nm). This T$_1$ energy is comparable to the one reported previously for monomeric Ga^{III}/Ln^{III} MCs (22 170 cm^{-1}) which is expected since the same ligands are involved in the formation of the [12-MC$_{Ga(III)shi}$-4] core in both series of complexes. In general the ligands-centered triplet state energy in [LnGa$_4$]$_2$ is higher than the accepting levels of most of the studied Ln^{III} ions (Pr, Nd, Sm, Eu, Tb, Dy, Ho, Er, Tm, and Yb,) being suitable for their sensitization. However, we can postulate that the T$_1$ energy is too close ($\Delta E < 2000$ cm^{-1}) to the accepting levels of Tb, Dy and Tm ions, increasing the probability of back energy transfer from the metal to the ligand.[8] Indeed, characteristic sharp bands arising from the lanthanide centered f–f transitions in the visible and/or NIR ranges could be detected for Pr, Nd, Sm, Tb, Dy, Ho, Er, and Yb MCs (Figure 4). However, upon ligand excitation Tm and Eu MCs do not exhibit any f–f transitions due to an inefficient energy transfer or a quenching effect caused by the presence of LMCT states, respectively.

In general, all studied complexes exhibit quantum yields and luminescence lifetimes comparable with the top values reported to date especially for NIR-emitting Ln^{III} ions.[8] Nevertheless, the values of τ_{obs} and Q_{Ln}^L of dimeric [LnGa$_4$]$_2$ complexes are lower than the corresponding ones reported for the monomeric LnGa$_4$.[2c] The only exception is the [TbGa$_4$]$_2$ complex that displays a strong green emission resulting from transitions between the $^5D_4$ and ^7F_J ($J = 0$–6) electronic levels, with the same quantum yield value within experimental error (31.2(2)% versus 34.7(1)%) and 1.3-fold longer luminescence lifetime
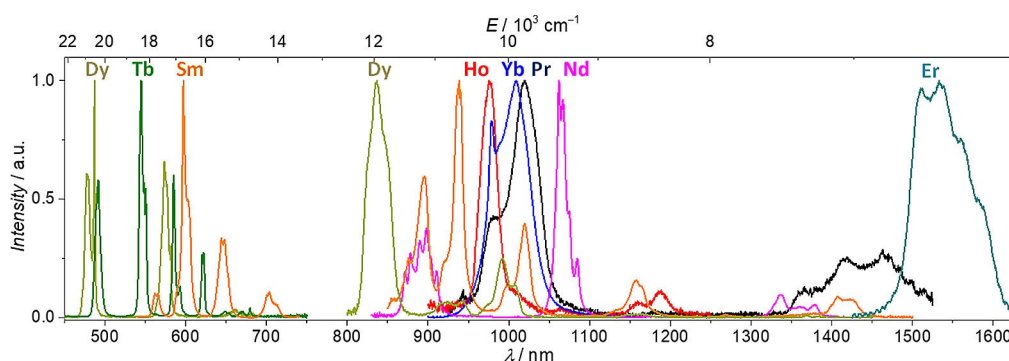

Figure 4. Corrected and normalized emission spectra of the [LnGa$_4$]$_2$ complexes in the solid state under ligand excitation at 350 nm at room temperature.

(1.410(1) ms versus 1.08(1) ms). It is worth noting here that the isolation of the [PrGa₄]₂ and [NdGa₄]₂ complexes, which were not obtained with the monomeric LnGa₄ series,[2c] and an observation of their characteristic emission completes the whole family of NIR emitting Ga^{III}/Ln^{III} MC complexes that is now also including Pr, Nd, Sm, Dy, Ho, Er, and Yb. There are only a few examples in the literature where NIR emission of the Pr^{III} and Ho^{III} complexes formed with chromophoric organic ligands could be detected and quantified.[3b,c,h,9] However, these signals were clearly identified for the [PrGa₄]₂ and [HoGa₄]₂ complexes (Figure 4 and Table 1). This again confirms the superiority of the MC approach toward the deration of highly luminescent Ln^{III}-based probes and materials.[2,4]

Table 1. Luminescence lifetimes (τ_{obs}) and absolute quantum yields (Q_{Ln}^{L}) of [LnGa₄]₂ complexes in the solid state at room temperature.[a]

Ln^{III}	τ_{obs} [μs][b]	Q_{Ln}^{L} [%][c]	
		Visible	NIR
Pr	0.901(6)	–	$9.3(1)\times10^{-3}$
Nd	2.46(1)	–	0.99(2)
Sm	117(1)	2.09(5)	0.269(3)
Tb	1410(1)	31.2(2)	–
Dy	15.0(1)	0.85(1)	$7.5(1)\times10^{-2}$
Ho	0.032(1)	–	$3.3(1)\times10^{-3}$
Er	5.23(2)	–	$5.7(1)\times10^{-3}$
Yb	30.5(1)	–	2.43(6)

[a] 2σ values are given between parentheses. Experimental relative errors: τ_{obs}, ±2%; Q_{Ln}^{L}, ±10%. [b] Under excitation at 355 nm upon monitoring the maxima of the main f–f transitions. [c] Upon excitation at 350 nm.

In order to rationalize the reasons which may explain the actual lowering of Q_{Ln}^{L} and τ_{obs} of the dimeric complexes compared to the corresponding monomeric LnGa₄ MCs, in the case of the [SmGa₄]₂ complex in the solid state, we determined the value of the intrinsic quantum yield, Q_{Sm}^{Sm}, which was found to be 3.7(1)% in the visible range under direct excitation into $^{4}G_{5/2}\leftarrow^{4}I_{9/2,\ 11/2}$ transitions at 480 nm. Thus, the sensitization efficiency, defined as the ratio between Q_{Sm}^{L} and Q_{Sm}^{Sm}, is $\eta_{sens}=2.09/3.7=0.57$ or 57%. Therefore, the sensitization ability of the MC scaffold in [SmGa₄]₂ is higher or comparable with the one observed in the case of the monomeric SmGa₄.[2c] It is worth mentioning here that in the composition of [LnGa₄]₂, NH_4^+ cations and H_2O molecules are present increasing the probability of non-radiative deactivations through N—H and O—H vibrations ($d_{Dy1\cdots O1}=4.69$ Å). In addition, the shorter distance between the Ln^{III} ions (7.2 Å) in [LnGa₄]₂ compared to the ones observed in the monomeric MCs (12.3–14.9 Å) (Figure S1), can possibly lead to a more efficient cross relaxation. However, in terms of brightness, which corresponds to the product of quantum yield and the molar absorptivity, a slightly lower quantum yield found for [LnGa₄]₂ compared to the value reported for the monomeric MC could be offset by doubling the molar absorptivity of the former one.

In conclusion, a new family of dimeric [LnGa₄]₂ metallacrown supramolecules was synthesized and fully characterized including an analysis of their emission properties in the visible and NIR domains. A specificity of the design of these MCs, in particular, their dimeric structure and the presence of the bridge, allow a broad variety of functionalization with chemical groups of different nature through carboxylate substitution. This advantage opens new perspectives for the design of molecules with desired properties for a wide range of applications. Physical analysis of the properties of these new MCs has shown that they do not dissociate in DMSO solutions. Photophysical studies have demonstrated that the MC scaffold in [LnGa₄]₂ is able to sensitize efficiently the characteristic emission of Nd, Pr, Sm, Tb, Dy, Ho, Er and Yb in the visible and/or NIR ranges in the solid state. In addition, [YbGa₄]₂ shows promising photophysical properties allowing us to observe epifluorescence signal in the NIR resulting from the non-specific interactions of MC aggregates on the surface of living HeLa cells (Figure S6). Furthermore, [YbGa₄]₂ has been proved to be non-cytotoxic in the studied range of concentrations (0–200 μM; Figure S5).

Conflict of interest

The authors declare no conflict of interest.

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