

143. Synthesis, Characterization, and Structural Properties of Luminescent Lanthanide Complexes

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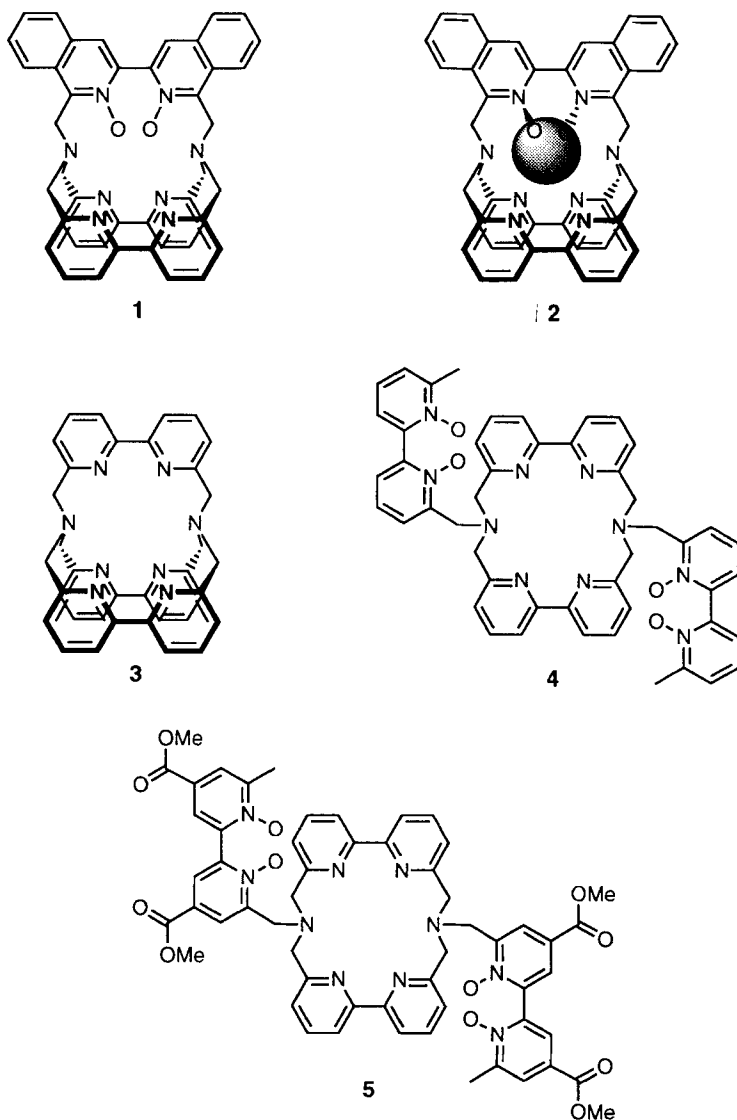
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The crystal structure of the macrobicyclic europium(III) complex $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$ incorporating a *N,N'*-dioxide unit has been determined. It confirms the cryptate nature of this species, the included cation being bound to six N- and two O-sites. The efficient shielding of the bound Eu^{3+} ion may be related to the efficient luminescence of this cryptate and points to the role played by the *N*-oxide sites. To further explore the effect of such binding groups, the two macrocyclic ligands **4** and **5** bearing two bipyridine *N,N'*-dioxide lateral arms have been synthesized and their Eu^{III} and Tb^{III} complexes prepared.

Europium cryptates of macrobicyclic ligands incorporating 2,2'-bipyridine (bpy) units have been shown to function as light-conversion device following an A-ET-E (absorption-energy transfer-emission process [1] [2]), presenting a strong luminescence from the complexed Eu^{III} ion under excitation of the ligand groups. In addition, these substances also present very interesting properties for use as luminescent labels for biological materials, e.g. monoclonal antibodies for fluoroimmunoassay (FIA) medical diagnostics, oligonucleotide sequences, etc. [3].

New developments involve the design of novel ligands to further improve the photo-physical properties, in particular for use in FIA. The synthesis of the EuCl_3 complex of the macrobicyclic ligand $[\text{bpy} \cdot \text{bpy} \cdot \text{biqiO}_2]$, **1**, incorporating bpy and 3,3'-biisoquinoline-2,2'-dioxide (biqiO₂) units, has been described previously [4]. The composition and spectral properties of its Na^+ and Eu^{3+} complexes agree with the cryptate **2** formulations $[\text{Na}^+ \subset \mathbf{1}]\text{Br}^-$ and $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$, respectively, the cation being located in the intramolecular cavity [4], as in the case of the parent complex $[\text{Eu}^{3+} \subset \mathbf{3}]\text{3Cl}^-$ containing no *N*-oxide site [1a, b]. The $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$ complex presents a strong emission in aqueous solution. In comparison to the europium cryptate of the parent macrobicyclic ligand **3**, the luminescence properties are markedly improved. This may be ascribed, at least in part, to the better shielding of the bound cation by the two O-atoms of the *N*-oxide sites in **1**. These results prompted us to design ligands incorporating more than one dioxide unit in order to achieve high luminescence.

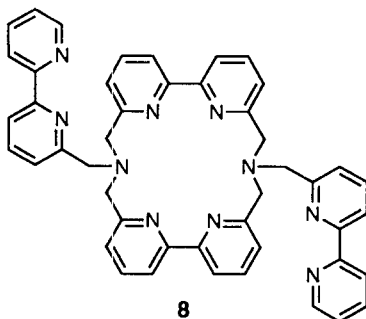
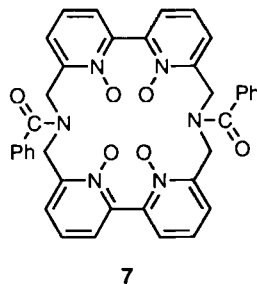
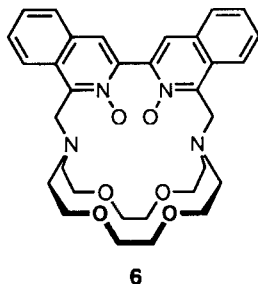
Thus, the new macrocyclic ligands **4** and **5**, containing two bpy units in the ring and two bpyO₂ groups in the branches, as well as different lanthanide(III) complexes of these ligands have been synthesized and characterized. The corresponding Eu^{3+} complexes showed an intense luminescence, potentially interesting for FIA applications.



The Eu^{3+} complexes of other ligands such as **6** [5a] and **7** [5b] incorporating *N,N'*-dioxide units have been described. In these cases, no solid-state structure was determined, and the luminescence was quenched by H_2O [5]. For the cryptate $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$, however, photophysical studies indicated a high quantum yield [6], higher than that of the parent complex $[\text{Eu}^{3+} \subset \mathbf{3}]\text{3Cl}^-$ [1b]. It appeared that the *N*-oxide groups of the former increased the ligand-to-metal energy-transfer efficiency [6]. Steric protection of the cation also enhanced the emission efficiency, since the cryptand structure hindered deactivation by interaction of the bound cation with H_2O molecules [7].

Structural information was required on the binding of the cation in the cavity, to better understand the improved photophysical properties of $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$ compared to $[\text{Eu}^{3+} \subset \mathbf{3}]\text{3Cl}^-$ and to be able to design new ligands constituting efficient labels for FIA.

We describe herewith the crystal structure of the complex $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$ as well as the synthesis and Eu^{3+} complexes of *N*-oxide derivatives of a branched macrocycle of type **8**, *i.e.*, of the macrocycle **4** and its substituted derivative **5**. The latter is suitable for attachment to a biological molecule.



Structure of the Cryptate $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$. – As expected, the crystal structure shows that the complex formed by EuCl_3 with the macrobicyclic ligand **1** is of cryptate type **2**, *i.e.*, $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$, where the Eu^{3+} cation is encapsulated in the molecular cavity. The Eu^{3+} cation displays nine-fold coordination: to six N-atoms, to two O-atoms, and to one other species, Cl^- .

The two bpy moieties (A and B) are raised like wings around the cation, and the $\text{biq}(\text{O})_2$ unit (C) is located on the opposite side along the binary axis (*Fig. 1, a*). The environment of the cation is more spherical for this complex $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$ than for the parent complexes $[\text{Ln}^{3+} \subset \mathbf{3}]\text{3Cl}^-$ ($\text{Ln} = \text{Tb}, \text{La}$) [8]. The spatial disposition of the wings A and B recalls the overall geometrical features of the structure of the $[\text{Li}^+ \subset \text{py} \cdot \text{biq} \cdot \text{biq}]$ cryptate [9] where the Li^+ ion was also buried inside the ligand and protected from the environment.

Contrary to the cryptates $[\text{Ln}^{3+} \subset \mathbf{3}]\text{3Cl}^-$, presenting two empty solid angles on two faces of the macrobicyclic and, therefore, allowing the anions or deactivating solvent molecules to have access to the cation through all three faces to complete the coordina-

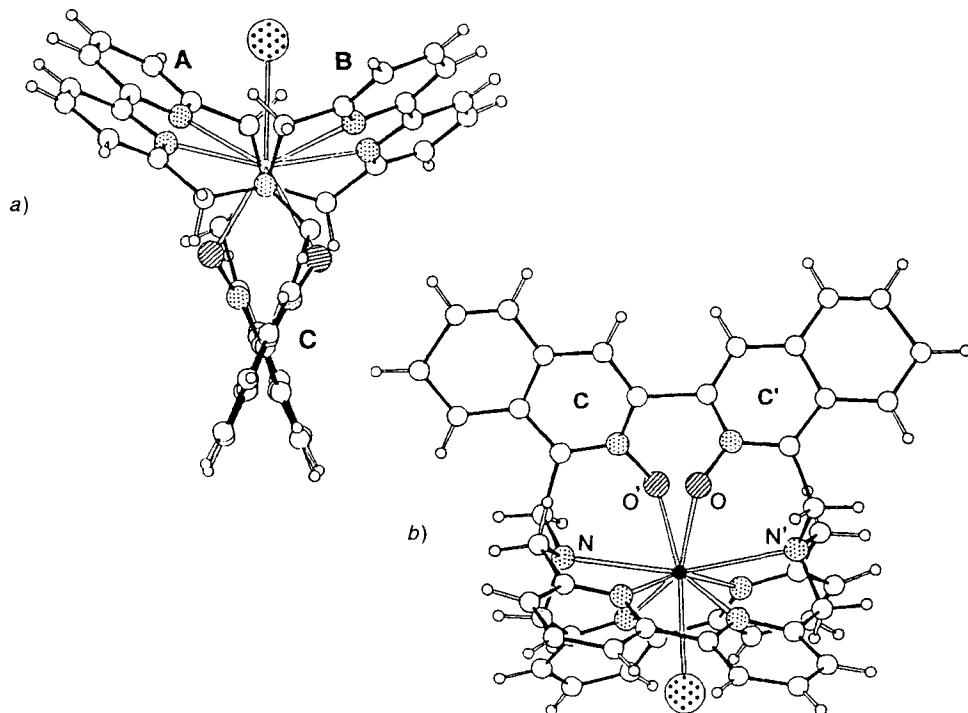


Fig. 1. Crystal structure of the $[Eu^{3+} \cdot 1]3Cl^{-}$ cryptate viewed a) along the N,N' axis and b) perpendicularly to it

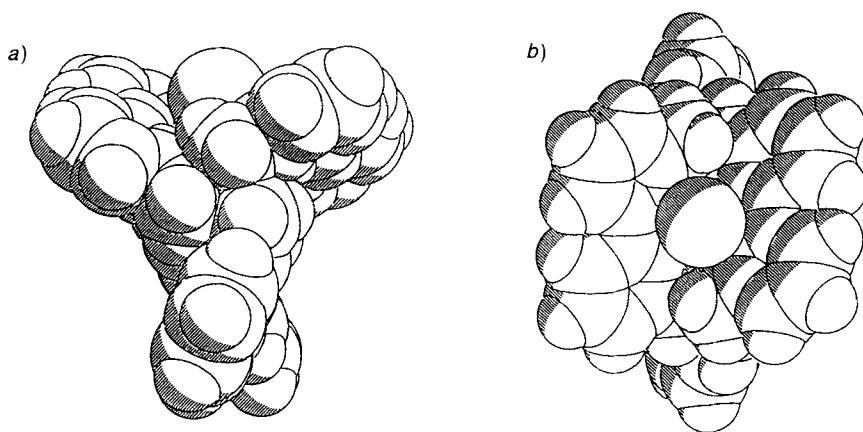


Fig. 2. Space-filling representation of the crystal structure of the Eu^{3+} cryptate of ligand 1 with the bound Cl^{-} ion viewed a) along the N,N' axis and b) down in the $Cl-Eu$ direction

tion shell [8], the present cryptate cation presents only one ‘open face’, while the solid angles on the other two faces of the macrobicycle **1** are protected by the O-atoms of the two *N*-oxide functions. Thus, the approach of anion or of solvent molecules is hindered. In addition, a Cl[−] anion occupies the unprotected space between bpy(A) and bpy(B) (Fig. 2) and occludes completely the small Eu³⁺ cation underneath.

The two pyridine moieties of each bpy are approximately coplanar, but the two moieties of the biqO₂ group are not. This is probably due to strong steric interference between the two O-atoms of the *N*-oxide units (Fig. 1).

The Eu³⁺ cation is located above the *N,N'* bridgehead axis, at a distance of 0.7 Å from the plane formed by the four bpy N-atoms. The N–Eu distances are slightly different for the various chelating N-atoms; the shortest are to N(bpy) (2.60 Å), whereas for the bridgehead N-atoms, the distance is 2.66 Å. The O–Eu distances to the O-atoms of the *N*-oxide units are even smaller (2.39 Å) (Table 1). Further selected interatomic distances and angles and the crystallographic data of [Eu³⁺ c 1]3Cl[−] are given in Tables 1–3.

Synthesis of Free Macrocyclic Ligand 4 and of Its Ln³⁺ Complexes. – The macrocyclic ligand **4** was synthesized from the intermediate macrocyclic unit **9** and its pendant arms. Oxidation of 6-(bromomethyl)-6'-methyl-2,2'-bipyridine [10] by treatment with 3-chloroperbenzoic acid in CHCl₃ gave the *N,N'*-dioxide **10** (71% yield), which was added dropwise to a solution of macrocycle **9** [11] in refluxing MeCN, in presence of Na₂CO₃, to give the NaBr complex of **4**. Washing this complex with H₂O removed the cation, and the free ligand **4** was obtained by chromatography in moderate yield (42%).

Lanthanide (Ln³⁺ = Eu³⁺, Tb³⁺, Gd³⁺) complexes of ligand **4** were prepared by treatment of the corresponding lanthanide(III) chloride in MeOH. The free ligand is insoluble in MeOH, but its lanthanide(III) complexes are very soluble in this solvent. The complexes had the composition [Ln(**4**)Cl₃]. Subsequent photophysical studies [2] revealed a

 Table 1. Selected Interatomic Distances for the Cryptate [Eu³⁺ c 1]3Cl[−]

	Distance [Å]		Distance [Å]
Eu–N(A)	2.606(8)	N(A)–C(2,A)	1.361(13)
Eu–N(A')	2.612(9)	N(A)–C(6,A)	1.304(15)
Eu–N(bridge)	2.681(9)	N(A')–C(2,A')	1.337(12)
Eu–O	2.388(6)	N(A')–C(6,A')	1.330(15)
Eu–Cl	2.772(3)	N(C')–C(3,C')	1.408(14)
N(C)–O	1.377(13)	N(C')–C(1,C')	1.284(18)
		C(3,C)–C(3,C')	1.465(18)

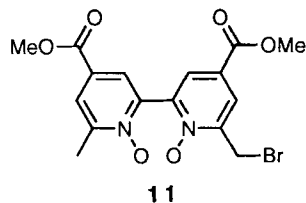
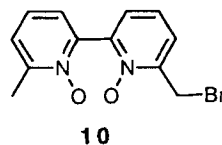
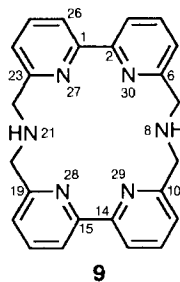
 Table 2. Selected Interatomic Angles for the Cryptate [Eu³⁺ c 1]3Cl[−]

	Angles [°]		Angles [°]
N–Eu–N(A)	62.1(2)	N(A)–Eu–N(A')	62.5(2)
N'–Eu–N(A')	64.1(2)	N(A)–Eu–N(B)	133.5(2)
N(A)–Eu–O'	80.8(2)	N(A')–Eu–O	117.8(2)
N–Eu–N'	161.9(2)	N(A')–Eu–N(B)	109.1(2)
O'–Eu–O	66.0(2)	N(A')–Eu–N(B')	160.4(2)

Table 3. Crystallographic Data^{a)} for the $[Eu^{3+} \subset \mathbf{1}]3Cl^-$ Complex

Formula	$(C_{44}H_{34}ClEuN_8O_2)^{2+}, 2Cl^-$		
Formula weight	965.1		
Crystals dimensions	$0.7 \times 0.5 \times 0.15 \text{ mm}^3$		
Space group	monoclinic $C2/c$		
a [Å]	13.956(6)	α [°]	90
b [Å]	28.66(1)	β [°]	109.1(1)
c [Å]	12.641(6)	γ [°]	90
V [Å ³]	4778(8)	D_x [g/cm ³]	1.34
Z	4	T [K]	294
μ [mm ⁻¹]	1.52	Max 2θ [°]	50
Scan range [°]	0.8	Scan speed [°/s]	0.025
Reflexions collected	3359	$F(000)$	1936
R	0.053	R_w	0.065

^{a)} Measured with a graphite crystal monochromatized ($\lambda = 0.7107 \text{ \AA}$) on an automated four-circle Philips diffractometer. $\omega/2\theta$ Data collection gave 3359 reflexions of which 2324 were independent and $> 3\sigma(I)$. Corrections were applied for Lorentz and polarization effects.



high luminescence quantum yield (comparable to that of the reference compound $[Eu^{3+} \subset \mathbf{3}]3Cl^-$) for complex $[Eu^{3+} \subset \mathbf{4}]3Cl^-$.

Ligand **5** has been synthesized by a stepwise procedure similar to the one used for the synthesis of **4**. Dimethyl 6-(bromomethyl)-6'-methyl-2,2'-bipyridine-4,4'-dicarboxylate [12] was oxidized to the corresponding N,N' -dioxide **11** by treatment with 3-chloroperbenzoic acid in $CHCl_3$ (68% yield). Dropwise addition of the substituted monobromo N,N' -dioxide **11** to a solution of macrocycle **9**, under conditions similar to those used in the synthesis of **4**, gave the NaBr complex of **5**. Pure free ligand **5** was obtained in low yield (21%) after washing of the crude NaBr complex with H_2O and crystallization from Et_2O /acetone. The lanthanide ($Ln^{3+} = Eu^{3+}, Tb^{3+}$) complexes of ligand **5** were prepared as described for **4**; they are also very soluble in MeOH.

Discussion. – The Eu^{3+} complex of the macrobicyclic ligand **1** acts as a more efficient molecular device for the conversion of UV into VIS red light [4] than $[Eu^{3+} \subset \mathbf{3}]3Cl^-$. This was ascribed to more effective protection of the Eu^{3+} cation in **1** against H_2O molecules.

However, a detailed analysis of the photophysical properties [6] showed that the Eu^{3+} ion in complex $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$ was still accessible to an average of 1.4 molecules of H_2O (as compared to *ca.* 9 in the uncomplexed cation and 2.5 in the parent complex $[\text{Eu}^{3+} \subset \mathbf{3}]\text{3Cl}^-$ [**1b**]). These results agree with the structure of the cryptate. As seen in *Figs. 1* and *2*, the ligand in the complex $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$ presents just one open solid angle for the H_2O molecules to access the encapsulated cation, which is partly occupied by the external chloride anion. Therefore, the significant gain in light-conversion efficiency may result from both more efficient ligand-to-metal energy transfer due to the introduction of *N*-oxide coordinating units and more efficient steric protection of the Eu^{3+} ion by those particular units.

The structural information obtained from these crystallographic data and the photophysical studies effected on such molecules [6] led to the design of luminescent cryptates of increased efficiency. A more effective shielding of the cation was expected upon introduction of a second *N,N'*-dioxide unit, able to block the third solid angle face of the system against the approach of H_2O molecules. This is the case of ligand **4** bearing two bpy *N,N'*-dioxide groups. Photophysical studies on the corresponding Eu^{3+} complex [2] showed that it displayed high luminescence efficiency and remarkable stability in H_2O [2], in contrast to the complex of **8** (containing no *N*-oxide functionalities) [12]. Moreover, since such complexes appeared to be interesting as luminescent labels, further elaboration involved the introduction in ligand **4** of functional groups for attachment to biological materials. This is the case in complex $[\text{Eu}^{3+} \subset \mathbf{5}]\text{3Cl}^-$ which is under investigation as FIA label [13].

Experimental Part

General. All reagents were commercial and used without purification. CHCl_3 was filtered over basic aluminium oxide (*Merck 90*, act. I). MeCN and CH_2Cl_2 were distilled over CaH_2 . Aluminium oxide: *Merck 90*, act. II–III. M.p.: uncorrected; digital melting-point apparatus, electrothermal. UV/VIS Spectra: *Cary-13* spectrophotometer. IR Spectra: *Perkin-Elmer-597* spectrometer; KBr pellets. NMR Spectra: *Bruker-SY 200* (200.1 (^1H) or 50.3 MHz (^{13}C)); $\delta(\text{H})$ in ppm rel. to residual protiated solvent in CDCl_3 (7.26), CD_2Cl_2 (5.32), or CD_3OD (3.30); $\delta(\text{C})$ in ppm rel. to the solvent CDCl_3 (77.03), CD_2Cl_2 (53.84), or CD_3OD (49.02). MS: fast-atom bombardment (FAB), positive mode *ZAB-HF* in 4-nitrobenzyl alcohol (NBA) or trifluoromethanesulfonic acid (TSA) matrix unless otherwise specified; EI = electron ionization. Elemental analyses were performed by the analytical services of the Institut de Chimie, Strasbourg.

Cryptate $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$ was synthesized as described in [4].

X-Ray Crystal Structure of $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$. Suitable crystals were obtained by adding Et_2O to a clear MeOH soln. of $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$. After two days of slow diffusion, orange micro-crystals appeared. These crystals showed strong red luminescence under UV light. A thin plate was used for the crystal-structure determination (see *Table 3*). Direct methods [14a] and full-matrix least squares [14b] on *F*: C, N, O, Cl, Eu anisotropic refinement to $R = 5.3\%$. Weighting scheme $w = [\sigma^2(F) + 0.002F^2]^{-1}$ (σ from counting statistics). The Eu^{3+} ion and its coordinated Cl^- are located on the same crystallographic binary axes. The second Cl^- (which is symmetry-doubled) is disordered in at least seven positions. The Eu^{3+} ion is encapsulated in the cage showing nine shortest distances with Cl (2.772(3) Å), N(A),N(A') (2.606(8) Å), N(B),N(B') (2.612(9) Å), O,O' (2.388(6) Å), and the two amino groups from the bridges N,N' (2.681(9) Å). So the cation Eu^{3+} (0.95 Å) is slightly too small for the size of the cavity but not as much as in the case of the prototype complex $[\text{Eu}^{3+} \subset \mathbf{1}]\text{3Cl}^-$, where the N-atoms form a circular cavity of 2.8 Å diameter.

6-(Bromomethyl)-6'-methyl-2,2'-bipyridine 1,1'-Dioxide (**10**). A stirred soln. of 6-(bromomethyl)-6'-methyl-2,2'-bipyridine [10] (0.5 g, 1.9 mmol) in CHCl_3 (100 ml) was cooled to 0° (ice bath). A soln. of 3- $\text{ClC}_6\text{H}_4\text{CO}_3\text{H}$ (55% aq.; 3.9 mmol) in CHCl_3 (50 ml) was added slowly. The mixture was allowed to warm to r.t., and 4 h later, another 0.5 g (55% aq.; 1.2 mmol) of 3- $\text{ClC}_6\text{H}_4\text{CO}_3\text{H}$ were added and stirred for 12 h (TLC monitoring).

Evaporation at 25° yielded **10**, which was washed thoroughly with Et₂O and dried *in vacuo*: yellow powder (0.4 g, 71%). M.p. 125° (dec.). TLC (Al₂O₃, 2% MeOH/CH₂Cl₂): R_f 0.3. UV/VIS (CH₂Cl₂): 318 (2900), 273 (14100). IR (KBr): 2946 (Me); 1478, 1446, 1426, 1395 (py); 1259, 1243 (N–O). ¹H-NMR (CDCl₃): 2.60 (s, Me); 4.70 (s, CH₂Br); 7.20–7.70 (*m*, 6 H, bpyO₂). ¹³C-NMR (CDCl₃): 18.1 (Me); 25.4 (CH₂Br); 126.4, 126.8, 127.0, 127.8, 128.5 (CH); 128.9 (C); 133.4, 133.5, 133.6 (C). EI-MS: 296 (*M*⁺), 280 ([*M* – O]⁺), 199 ([*M* – O – Br]⁺). Anal. calc. for C₁₂H₁₁BrN₂O₂ (295.13): C 48.83, H 3.76, N 9.49; found: C 48.86, H 3.99, N 9.10.

6,6'-(8,21,27,28,29,30-Hexaazapentacyclo[21.3.1.1^{2,6}.1^{10,14}.1^{15,19}]triacenta-1(27),2,4,6(30),10,12,14(29),15,17,19(28),23,25-dodecaene-8,21-diyl)bis[6'-methyl-2,2'-bipyridine] 1,1',1'',1'''-Tetraoxide (= 8,21-Bis(6'-methyl-2,2'-bipyridin-6-yl)-8,21,27,28,29,30-hexaazapentacyclo[21.3.1.1^{2,6}.1^{10,14}.1^{15,19}]triacenta-1(27),2,4,6(30),10,12,14(29),15,17,19(28),23,25-dodecaene N,N',N'',N'''-Tetraoxide) (**4**). Compound **10** (1.1 g, 3.70 mmol) in 200 ml of freshly distilled MeCN was added slowly to a stirred refluxing mixture of macrocycle **9** [10] (450 mg, 1.14 mmol) and Na₂CO₃ (3 g, 28.30 mmol) in dry MeCN (300 ml) under N₂. Vigorous stirring at reflux was continued for 24 h. The hot mixture was filtered and the filtrate evaporated at r.t. This powder was dissolved in CHCl₃ (200 ml). The org. phase was washed 3 × with distilled H₂O to eliminate the included NaBr salt, dried (MgSO₄), and evaporated. Chromatography (Al₂O₃, 10% MeOH/CH₂Cl₂) yielded pure free ligand **4** (42%). Pale yellow powder. M.p. 235° (dec.). TLC (difficult to determine because of the exchange between the free ligand and the NaBr complex). UV/VIS (CH₂Cl₂): 276 (75000). IR (KBr): 2929 (Me); 1571, 1442, 1430, 1376 (py); 1267 (N–O). ¹H-NMR (CDCl₃): 2.59 (s, 2 Me); 4.21 (s, 8 H, CH₂); 4.55 (s, 4 H, CH₂); 7.09 (*d*, *J* = 7.3, 4 H); 7.31–7.47 (*m*, 14 H); 7.74 (*d*, *J* = 7.5, 4 H); 8.22–8.27 (*m*, 2 H). ¹³C-NMR (CDCl₃): 18.1 (2 Me); 58.2 (2 CH₂); 62.0 (4 CH₂); 121.2, 124.9, 125.5, 127.7, 128.1, 128.5, 130.8, 139.3 (24 C); 145.3, 145.4, 148.8, 150.4, 156.0, 159.9 (16 C). FAB-MS (NBA): 845.1 ([*M* + Na]⁺), 823.1 ([*M* + H]⁺), 807.1 ([(*M* – O) + H]⁺). Anal. calc. for C₃₈H₄₄N₁₀O₄·H₂O (840.91): C 68.55, H 5.27, N 16.66; found: C 68.34, H 5.09, N 16.38.

Dimethyl 6-(Bromomethyl)-6'-methyl-2,2'-bipyridine-4,4'-dicarboxylate 1,1'-Dioxide (**11**). A stirred soln. of dimethyl 6-(bromomethyl)-6'-methyl-2,2'-bipyridine-4,4'-dicarboxylate [12] (0.75 g, 1.9 mmol) in CHCl₃ (100 ml) was cooled to 0° (ice bath). A soln. of 3-ClC₆H₄CO₂H (55% aq.; 13.1 mmol) in CHCl₃ (100 ml) was added slowly. The mixture was allowed to warm to r.t. After 10 h, another portion of 3-ClC₆H₄CO₂H (55% aq.; 13.1 mmol) was added and stirred for 10 h (TLC monitoring). This was repeated six times. Evaporation at 25° yielded **11** which was washed thoroughly with Et₂O and dried *in vacuo*: yellow powder (68%). M.p. 241° (dec.). TLC (silica gel, 2% MeOH/CH₂Cl₂): R_f 0.3. UV/VIS (CH₂Cl₂): 298 (32500). IR (KBr): 2925 (Me); 1717 (CO₂Me); 1437 (py); 1272 (N–O). ¹H-NMR (CDCl₃): 2.58 (s, Me); 3.96 (s, CO₂Me); 4.71 (s, CH₂Br); 8.08 (*d*, *J* = 2.4, 1 H, py); 8.24 (*d*, *J* = 2.5, 1 H, py). ¹³C-NMR (CDCl₃): 17.9 (Me); 25.1 (CH₂Br); 52.9, 53.1 (MeO); 126.1, 127.2, 127.4, 127.7 (CH); 142.5, 143.8, 148.3, 150.1 (C); 163.6, 164.0 (C=O). EI-MS: 411.0 (*M*⁺), 331.0 ([*M* – Br]⁺). Anal. calc. for C₁₆H₁₅BrN₂O₆ (411.21): C 46.73, H 3.68, N 6.80; found: C 46.52, H 3.54, N 6.53.

6,6'-(8,21,27,28,29,30-Hexaazapentacyclo[21.3.1.1^{2,6}.1^{10,14}.1^{15,19}]triacenta-1(27),2,4,6(30),10,12,14(29),15,17,19(28),23,25-dodecaene-8,21-diyl)bis[methyl 6'-methyl-2,2'-bipyridine-4-carboxylate] 1,1',1'',1'''-Tetraoxide (**5**). As described for **4**, with **11** (0.4 g, 0.97 mmol), MeCN (150 ml), macrocycle **9** [10] (175 mg, 0.44 mmol), Na₂CO₃ (1.4 g, 13.21 mmol), and MeCN (100 ml; 48 h). Workup with CHCl₃ (100 ml). The crude residue was thoroughly washed with Et₂O and acetone: **5** (21%). White powder. M.p. 205° (dec.). TLC: R_f difficult to determine because of the exchange between the free ligand and the NaBr complex. UV/VIS (CH₂Cl₂): 285 (118000). IR (KBr): 2961 (Me); 1717 (CO₂Me); 1653, 1437 (py); 1280 (N–O). ¹H-NMR (CDCl₃): 2.63 (s, 2 Me); 3.96 (s, 2 MeO); 3.98 (s, 2 MeO); 4.19 (s, 4 CH₂ of macrocycle); 4.51 (s, 2 CH₂ of arms); 7.14 (*d*, *J* = 7.2, 4 H); 7.37 (*t*, *J* = 7.6, 4 H); 7.76 (*d*, *J* = 7.5, 4 H); 8.04 (s, 4 arom. H of arms); 8.08 (*d*, *J* = 2.6, arom. H of arms); 8.79 (*d*, *J* = 2.6, arom. H of arms). ¹³C-NMR (CDCl₃): 17.9 (2 Me); 53.0 (2 MeO); 57.6 (2 CH₂ of arms); 64.1 (4 CH₂ of macrocycle); 118.9 (C). FAB-MS (NBA): 1077.2 ([*M* + Na]⁺), 1055.2 ([*M* + H]⁺), 1038.2 ([(*M* – O) + H]⁺), 1021.2 ([(*M* – 2 O) + H]⁺). Anal. calc. for C₅₆H₅₀N₁₀O₁₂·5 H₂O (1144.14): C 58.74, H 5.24, N 12.23; found: C 58.85, H 4.62, N 11.88.

Complex [Eu³⁺ + 4/3Cl⁻]. EuCl₃·6 H₂O (17 mg, 4.6·10⁻⁵ mol) was added to a stirred soln. of **4** (37 mg, 4.5·10⁻⁵ mol) in MeOH (15 ml) at r.t. (**4** not soluble, but Eu³⁺ complex very soluble). Vigorous stirring was continued for further 48 h. Et₂O (30 ml) was added, resulting in the formation of a white precipitate which was isolated after centrifugation: white powder (99%). M.p. 190° (dec.). TLC: no migration. UV/VIS (H₂O): 314 (19400), 259 (35600), 235 (49600). IR (KBr): 1657, 1626, 1577, 1482, 1450, 1435 (py); 1248, 1216 (N–O). ¹H-NMR (D₂O, rel. to ¹BuOH (1.36 ppm)): -2.53 (*d*, *J* = 7.0, 2 H); -0.34 (*d*, *J* = 7.9, 2 H); 0.09 (*d*, *J* = 7.5, 4 H); 1.93 (*d*, *J* = 7.3, 2 H); 3.01 (s, 2 H, CH₂); 3.93 (s, 6 H); 4.70 (*t*, *J* = 7.5, 2 H); 5.39 (*t*, *J* = 7.8, 2 H, CH₂); 5.75 (*t*, *J* = 7.1, 2 H); 6.54 (*t*, *J* = 8.4, 2 H); 6.94 (s, 2 H, CH₂); 7.72 (*d*, *J* = 7.8, 2 H); 7.80 (*d*, *J* = 7.5, 2 H); 9.53 (*d*, *J* = 7.5, 2 H); 10.59 (s, 2 H, CH₂); 21.00 (s, 2 H, CH₂); 26.48 (s, 2 H, CH₂). FAB-MS (NBA): 1045.0 ([*M* + Eu + 2 Cl]⁺), 1010.1 ([*M* + Eu + Cl]⁺), 994.1 ([(*M* – O) + Eu + Cl]⁺). Anal. calc. for C₄₈H₄₂N₁₀O₄·EuCl₃·4 CH₃OH·4 H₂O (1280.30): C 48.74, H 5.15, N 10.93; found: C 48.71, H 4.94, N 10.89.

Complex $[Tb^{3+} \subset 4]3Cl^-$. As described for $[Eu^{3+} \subset 4]3Cl^-$, with $TbCl_3 \cdot 6 H_2O$ (12 mg, $3.2 \cdot 10^{-5}$ mol), **4** (25 mg, $3.04 \cdot 10^{-5}$ mol), and MeOH (15 ml): white powder (94%). M.p. 190° (dec.). TLC: no migration. UV/VIS (H_2O): 309 (14300), 256 (25500), 230 (35000). IR (KBr): 1653, 1646, 1602, 1576, 1457, 1447, 1419 (py); 1249, 1219 (N–O). 1H -NMR (D_2O , rel. to 4BuOH (1.36 ppm)): –239.26 (s, 2 H); –221.21 (s, 4 H); –211.73 (s, 2 H); –48.76 (s, 2 H); –30.22 (s, 6 H); –10.29 (s, 2 H); 1.13 (s, 2 H); 3.55 (s, 2 H); 4.19 (s, 2 H); 7.93 (s, 2 H); 29.07 (s, 2 H); 48.44 (s, 2 H); 59.86 (s, 2 H); 66.85 (s, 2 H); 108.95 (s, 4 H); 109.47 (s, 2 H); 134.72 (s, 2 H). FAB-MS (NBA): 1050.9 ($[M + Tb + 2 Cl]^+$), 1014.9 ($[M + Tb + Cl]^+$). Anal. calc. for $C_{48}H_{42}O_4N_{10} \cdot TbCl_3 \cdot H_2O$ (1106.19): C 52.11, H 4.01, N 12.66; found: C 51.83, H 4.22, N 12.28.

Complex $[Gd^{3+} \subset 4]3Cl^-$. As described for $[Eu^{3+} \subset 4]3Cl^-$, with $GdCl_3 \cdot 6 H_2O$ (12 mg, $3.2 \cdot 10^{-5}$ mol), **4** (24 mg, $2.9 \cdot 10^{-5}$ mol), and MeOH (15 ml): white powder (96%). M.p. 185° (dec.). TLC: no migration. UV/VIS (H_2O): 307.5 (24400), 256.5 (30300), 231 (39700). IR (KBr): 1601, 1481, 1437, 1419, 1384 (py); 1250, 1218 (N–O). FAB-MS (NBA): 1050.0 ($[M + Gd + 2 Cl]^+$), 1014.0 ($[M + Gd + Cl]^+$), 836.0 ($[(M - 1 \text{ arm}) + 2 Gd]^+$), 798.0 ($[(M - 1 \text{ arm}) + Gd]^+$). Anal. calc. for $C_{48}H_{42}N_{10}O_4 \cdot GdCl_3 \cdot 8 H_2O$ (1230.63): C 46.80, H 4.58, N 11.38; found: C 46.81, H 4.48, N 10.76.

Complex $[Eu^{3+} \subset 5]3Cl^-$. As described for $[Eu^{3+} \subset 4]3Cl^-$, with $EuCl_3 \cdot 6 H_2O$ (19.5 mg, $5.3 \cdot 10^{-5}$ mol), **5** (51 mg, $4.8 \cdot 10^{-5}$ mol), and MeOH (40 ml). Precipitation with Et_2O (60 ml) and centrifugation: white powder (79%). M.p. 259° (dec.). TLC: no migration. UV/VIS (H_2O): 277 (49000). IR (KBr): 2940 (Me); 1734, 1717 (CO_2Me); 1734, 1717, 1653, 1646, 1600, 1457, 1437 (py); 1260, 1233 (N–O). 1H -NMR (D_2O , rel. to 4BuOH (1.36 ppm)): –1.09 (s, 2 H); 0.19 (s, 2 H); 0.53 (s, 1 H); 2.76 (s, 2 H); 3.08 (s, 8 H); 4.15 (s, 2 H); 4.16 (s, 2 H); 4.18 (s, 6 H); 5.29 (s, 2 H); 5.60 (s, 2 H); 5.90 (s, 1 H); 7.29 (s, 2 H); 8.19–8.65 (m, 5 H); 9.84 (s, 2 H); 21.30 (s, 1 H); 22.72 (s, 2 H). FAB-MS (NBA): 1277.1 ($[M + Eu + 2 Cl]^+$), 1242.1 ($[M + Eu + Cl]^+$), 947.0 ($[(M - 1 \text{ arm}) + Eu + 2 Cl]^+$), 542.0 ($[(bpy \cdot bpy) + Eu]^+$). Anal. calc. for $C_{56}H_{50}N_{10}O_{12} \cdot EuCl_3 \cdot 6 H_2O$ (1420.31): C 47.31, H 4.36, N 9.85; found: C 47.30, H 4.34, N 9.42.

Complex $[Tb^{3+} \subset 5]3Cl^-$. As described for $[Eu^{3+} \subset 4]3Cl^-$, with $TbCl_3 \cdot 6 H_2O$ (7.9 mg, $2.1 \cdot 10^{-5}$ mol), **5** (22 mg, $1.9 \cdot 10^{-5}$ mol), and MeOH (20 ml). Precipitation with Et_2O (20 ml) and centrifugation: white powder (88%). M.p. 264° (dec.). TLC: no migration. UV/VIS (H_2O): 285 (32000). IR (KBr): 2940 (Me); 1722 (CO_2Me); 1722, 1602, 1437, 1345 (py); 1262, 1234 (N–O). 1H -NMR (D_2O , rel. to 4BuOH (1.36 ppm)): very br. peaks. FAB-MS (NBA): 1282.8 ($[M + Tb + 2 Cl]^+$), 1246.8 ($[M + Tb + Cl]^+$), 952.8 ($[(M - 1 \text{ arm}) + Tb + 2 Cl]^+$). Anal. calc. for $C_{56}H_{50}N_{10}O_{12} \cdot TbCl_3 \cdot 6 H_2O$ (1427.27): C 47.08, H 4.34, N 9.80; found: C 46.77, H 4.07, N 8.97.

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