10. Synthesis and Properties of Acyclic and Cryptate Europium(III) Complexes Incorporating the 3,3'-Biisoquinoline 2,2'-Dioxide Unit

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The lithium and europium(III) cryptates of a macrobicyclic ligand **1** incorporating the 3,3'-biisoquinoline 2,2'-dioxide **2** have been prepared. The Eu(III) complex [Eu(**2**)$_2$]Cl$_3$ has also been obtained. These Eu(III) complexes present characteristic ^{1}H-NMR spectra containing markedly shifted resonances. They are strongly luminescent; the emission spectra, quantum yields, and lifetimes have been determined.

A number of macrocyclic [1–6] and macrobicyclic [2] [3] [7–9] ligands incorporating heterobiaryls (such as 2,2'-bipyridine, 3,3'-biisoquinoline, 2,2'-bipyrimidine) have been synthesized recently. They may be expected to form inclusion complexes with a variety of metal ions [2–4] [7]. Of particular interest is the ability of macrobicyclic ligands of this type to bind lanthanide cations, yielding photoactive cryptates that display strong luminescence and are of interest both as new luminescent materials and as potential labels for time-resolved photo-immunoassays [10–13].

The luminescence of such Eu(III) and Tb(III) cryptates takes place *via* an absorption/energy transfer/emission sequence [10–13]: the energy of the singlet excited state S$_1$ obtained upon light absorption by the heterocyclic unit is transferred in a radiationless process through the triplet state T$_1$ to the resonant level of the lanthanide ion which emits its characteristic visible light. Among bis-heterocyclic units, 3,3'-biisoquinoline (biqi) is itself strongly fluorescent, thus loosing its excited-state energy by light emission so that ligands incorporating this unit [3] gave only weakly luminescent lanthanide cryptates [14]. On the other hand, it has been well documented that heterocyclic N-oxides form lanthanide complexes that possess a particularly strong luminescence [15–17].

We thus initiated a general investigation into the preparation and luminescent properties of the lanthanide cryptates of macrocyclic and macrobicyclic ligands containing heterocyclic N-oxide groups. In particular, it was of interest to study the properties of the lanthanide cryptates of ligands containing the 3,3'-biisoquinoline 2,2'-dioxide ((biqi)O$_2$) unit. We report here the preparation of the lithium cryptate of the macrobicyclic ligand **1** and some photophysical properties of its Eu(III) cryptate together with the related data for the Eu(III) complex of the subunit 1,1'-dimethyl-3,3'-biisoquinoline 2,2'-dioxide (**2**) itself.

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Synthesis of the *N*-Oxide Ligands and of their Complexes. – Reaction of 1,1'-dimethyl-3,3'-biisoquinoline (**3**) [3] with *N*-bromosuccinimide in CCl₄ gave the bis(bromomethyl) derivative **4** [3] which was oxidized to the corresponding *N,N'*-dioxide **5** by treatment with 3-chloroperbenzoic acid (3-ClC₆H₄CO₃H) in CHCl₃ (65% yield). Condensation of **5** with the [18]-N₂O₄ macrocycle **6** [18] in presence of Li₂CO₃ and LiBr gave the LiBr complex of the macrobicyclic *N,N'*-dioxide **1** which was purified by column chromatography (37% yield of [Li(**1**)]Br). Oxidation of **3** [3] with 3-ClC₆H₄CO₃H in CHCl₃ afforded the corresponding *N,N'*-dioxide **2**.

The Eu(III) complexes were prepared by treatment of [Li(**1**)]Br and **2** with EuCl₃ or Eu(ClO₄)₃ in MeCN or MeOH in presence of triethyl orthoformate. The complexes obtained had the compositions [Eu(**1**)](ClO₄)₃ and [Eu(**2**)₂]Cl₃.
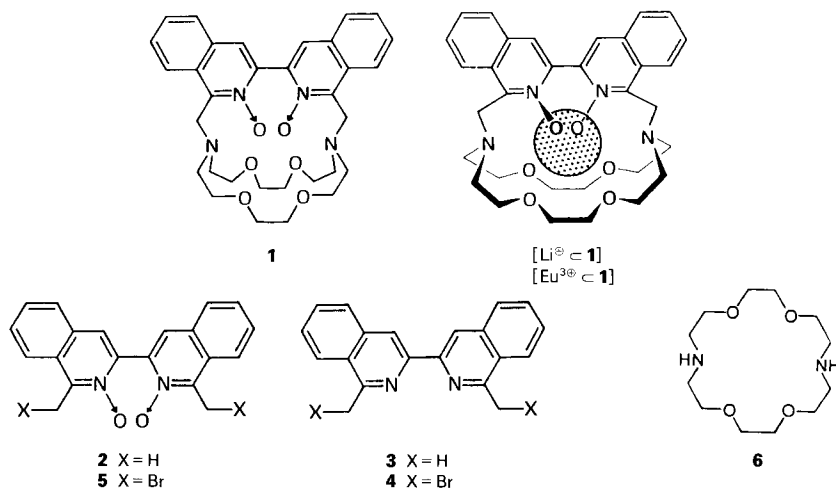
Structure and Properties of the Cryptates of 1 and of the Eu(III) Complex of 2. – The lithium complex [Li(**1**)]Br was soluble in MeCN, CHCl₃, and EtOH. Its composition and ¹H-NMR spectrum *(Fig. 1)* agree with the formulation of this compound as a cryptate [Li⁺ ⊂ **1**]Br⁻ in which Li⁺ is contained in the intramolecular cavity, as for the cryptates of related macrobicyclic ligands [2] [3] [7]. Although Li⁺ is smaller than the cavity of a macrobicyclic structure such as **1** [19], the presence of the inward directed *N*-oxide groups decreases cavity size and should allow stronger binding of this small cation than would otherwise be expected. The ¹H-NMR spectrum of [Li(**1**)]Br displays a well defined *AB* system for the biqi-C*H*₂N protons at *ca.* 4.20 and 4.63 ppm (*J* = 12.5 Hz). The complicated *multiplets* observed in the 2.6–4.1 ppm region show that the protons of the other CH₂ groups are also non-equivalent. These data indicate that the structure of the complex is twisted and rigid, torsional motions in the biqiO₂ unit and around the *N,N'*-bridgehead axis being slow on the NMR time scale. Such twisting and motions have been reported earlier for other macrobicyclic cryptates containing bpy or phen groups [2] [7].

A cryptate structure [Eu³⁺ ⊂ **1**] was also assigned to the Eu(III) complex of ligand **1** on the basis of the formation of La(III) and Eu(III) cryptates with related macrobicyclic
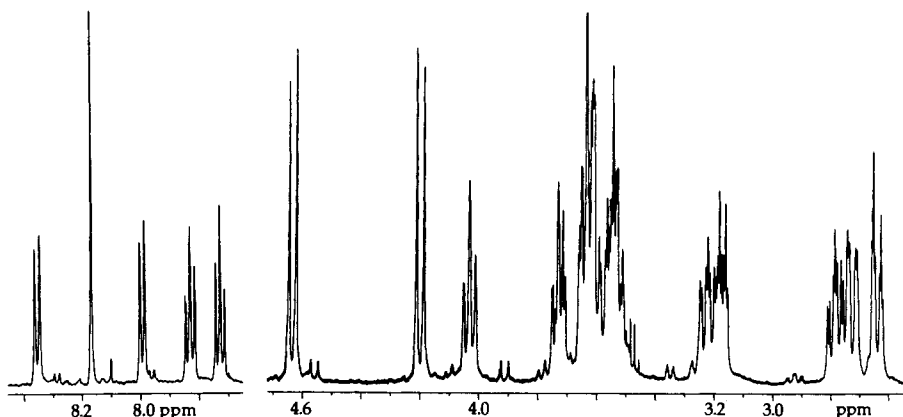
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Fig. 1. *500-MHz ^{1}H-NMR spectrum* (CDCl$_3$) *of the lithium cryptate [Li$^+$ ⊂ 1] Br$^-$.* The small signals could be due to the presence of some sodium cryptate formed by exchange during the isolation of the compound.

ligands [10], as confirmed by crystal-structure determinations [20]. The ^{1}H-NMR of [Eu(1)](ClO$_4$)$_3$ in CD$_3$CN presents very strongly shifted and broadened signals when compared with [Li(1)]Br, covering a wide domain from −19 to +14 ppm. With the data available, it is not possible to assign the signals. Widely spread out spectra have been observed for other Eu(III) cryptates, the shifts being larger and the signals broad in organic solvents as compared to aqueous solutions [10] [14].

The microanalysis of the Eu(III) complex formed by **2** indicated a Eu(III)(2)$_2$ stoichiometry. The presence of only two ligand molecules may be due to steric hindrance of the Me groups. With 2,2′-bipyridine *N,N′*-dioxide (bpyO$_2$), lanthanide complexes containing four ligand molecules have been obtained [15–17] [21–23]. The ^{1}H-NMR spectrum of [Eu(2)$_2$Cl$_3$] in CD$_3$CN presents broad peaks in the −2 to +10 ppm range. The structure of this complex has been determined by X-ray crystallography which indicates that Eu^{3+} is bound to the 4 O-atoms and the 3 Cl-anions [24].

Luminescence Properties of the Eu(III) Complexes [Eu^{3+} ⊂ 1]3ClO$_4^-$ and [Eu(2)$_2$Cl$_3$]. – Both the cryptate [Eu^{3+} ⊂ 1]3ClO$_4^-$ and the acyclic complex [Eu(2)$_2$Cl$_3$] showed the strong red luminescence characteristic of the Eu(III) emission when excited at 337 nm into the absorption of the heterocyclic *N*-oxide ligand. The emission spectra were those expected for Eu(III) complexes (*Figs. 2* and *3*).
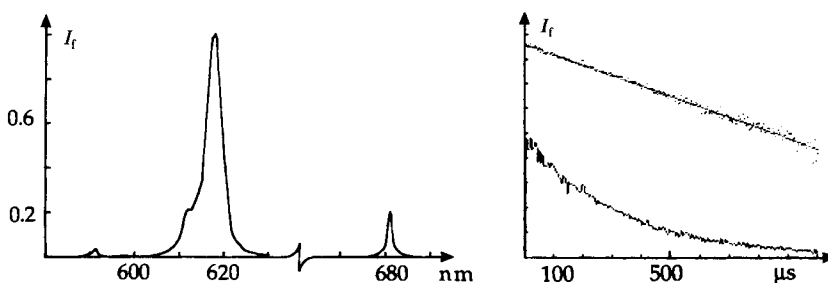

Fig. 2. *Luminescence spectrum* (left) *and luminescence decay* (right) *of the europium complex [Eu(2)$_2$Cl$_3$] in MeCN*
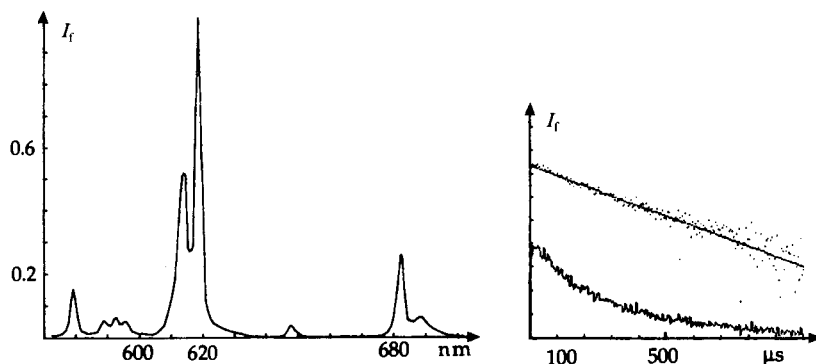
Fig. 3. *Luminescence spectrum* (left) *and luminescence decay* (right) *of the europium cryptate [Eu³⁺ ⊂ 1]3ClO₄⁻ in MeCN*

The quantum yield for [Eu(2)₂Cl₃] was evaluated by the method of *Haas* and *Stein* [25] using [Ru(bpy)₃]²⁺ as reference [26]. A highly efficient conversion, with a quantum yield of *ca.* 25%, of the absorbed UV light (*ca.* 340 nm) into Eu(III) luminescence was observed in MeCN. It is noteworthy that addition of a 3rd equiv. of ligand **2** to the complex solution did not lead to fluorescence enhancement, indicating that the 1:2 complex [Eu(2)₂Cl₃] was the predominant species. However, addition of H_2O (4% *v/v*) resulted in total fluorescence quenching. The fluorescence lifetime of [Eu(2)₂Cl₃] in i-PrOH solution was obtained from the decay of the emission at 618 nm after nitrogen-laser excitation at 337 nm. The decay was found to be exponential with a lifetime $\tau = 650 \pm 10$ µs *(Fig. 2)*.

The emission and excitation spectra of the [Eu³⁺ ⊂ 1]3ClO₄⁻ cryptate were similar to those observed for [Eu(2)₂Cl₃] with, however, somewhat different band structure *(Fig. 3)*. A total quantum yield of 4% was obtained for absorbed UV to VIS light conversion. The exponential decay *(Fig. 3)* gave a luminescence lifetime of 640 ± 20 µs.

One may note that both complexes studied here, [Eu³⁺ ⊂ 1]3ClO₄⁻ and [Eu(2)₂Cl₃], have long lifetimes as well as high UV-to-VIS conversion efficiency. These properties make the present and related complexes attractive light conversion molecular devices [10–13] of interest as novel luminescent species and as potential labels for time-resolved fluo-immunoassays. Further developments along these lines are in progress.

Experimental Part

General. All reagents were commercial and used without purification. MeCN was distilled over CaH_2; $CHCl_3$ over P_2O_5 and CaH_2. M.p.: uncorrected. UV spectra $((\lambda)(\varepsilon))$: *SPECORD M40*. IR spectra (cm⁻¹): *Beckman* spectrometer. NMR spectra: *Bruker-WP-200* and *AM-500-MHz* spectrometers in $CDCl_3$ or CD_3CN soln. with TMS as standard; chemical shifts in ppm, coupling constants in Hz. MS: *ZAB-HF*.

Fluorescence Measurements. Spectrofluorimeter constructed by *Jasny* [27]; wavelengths in nm. MeCN and i-PrOH were of spectrofluorimetric grade from *Merck*. The samples were not deoxygenated. Luminescence lifetimes for Eu(III) emission were measured after excitation of the sample in MeCN soln. with a pulse at 337 nm of an *IGT 50* nitrogen laser *(ZWG, GDR)* with the FWHM of 0.6 ns. The luminescence from the sample was collected in perpendicular geometry on the entrance slit of the *Jasny-M32* prism monochromator. The luminescence decay was observed at 618 nm. The signal from the photomultiplier *(RCA 1P28)*, after passing through a delay line, was processed by a *BCI-280* boxcar *(ZWG)* and then directed into a microcomputer. The decay time of the Eu(III)

luminescence was represented by a semilogarithmic plot. For quantum-yield determination, a soln. of [Ru-(bipy)₃]Cl₂ in H₂O deaerated by a stream of Ar, was used as standard. The error of quantum-yield measurements was estimated to be ±20%.

1,1'-Dimethyl-3,3'-biisoquinoline 2,2'-Dioxide (**2**). A suspension of 1,1'-dimethyl-3,3'-biisoquinoline (**3**; 2.84 g, 10 mmol) in CHCl₃ (100 ml) was treated with 3-ClC₆H₄CO₃H (80%; 6.46 g, 30 mmol) at 0° until disappearance of the starting material (TLC, Al₂O₃, MeOH/CHCl₃ 1:99). The clear soln. was evaporated at 25° and the residue washed with Et₂O to remove excess 3-ClC₆H₄CO₃H and 3-ClC₆H₄CO₂H. The crude product was crystallized from AcOEt: 87% of **2**, white microcrystals. M.p. 256° (dec.). UV (CHCl₃): 313 (2700), 305 (2600). IR (KBr): 1270, 900. ¹H-NMR (CDCl₃): 2.96 (*s*, 2 CH₃); 7.54–7.72 (*m*, 6 H); 7.78 (*d*, 2 H); 8.00 (*d*, 2 H). EI-MS: 316 (*M⁺*), 300, 284 (100), 269. Anal. calc. for C₂₀H₁₆N₂O₂ (316.40): C 75.93, H 5.09, N 8.85; found: C 75.77, H 4.97, N 8.60.

1,1'-Bis(bromomethyl)-3,3'-biisoquinoline 2,2'-Dioxide (**5**). A soln. of 1,1'-bis(bromomethyl)-3,3'-biisoquinoline [3] (**4**; 835.8 mg, 1.9 mmol) in boiling CHCl₃ (750 ml) was cooled to r.t. and protected from light. Then, 3-ClC₆H₄CO₃H (80%; 1304 mg, 7.6 mmol) was added and stirring maintained at r.t. for 3 days. Evaporation at 25° yielded **5** which was washed thoroughly with Et₂O and dried *in vacuo:* 582 mg (65%). Further purification by crystallization from THF. M.p. 248° (dec.). ¹H-NMR (CDCl₃): 5.25 (*s*, 2 CH₂Br); 7.65 (*t, J* = 7.4, 2 H); 7.80 (*t, J* = 7.4, 2 H); 7.85 (*d, J* = 8.65, 2 H); 7.98 (*s*, 2 H); 8.00 (*d, J* = 8.65, 2 H). Anal. calc. for C₂₀H₁₄Br₂N₂O₂ (474.10): C 50.67, H 2.97, Br 33.71, N 5.90; found: C 50.28, H 2.69, Br 35.76, N 5.63.

{1,1'-[N,N':N,N'-Bis(3,6-dioxaoctamethylene)bis(aminomethyl)]-3,3'-biisoquinoline 2,2'-Dioxide}lithium Bromide ([Li⁺ ⊂ **1**]Br⁻). Compound **5** (208.2 mg, 0.43 mmol) was added to a stirred and boiling mixture of **6** [18] (115 mg, 0.43 mmol), Li₂CO₃ (325 mg, 4.3 mmol), and LiBr (19 mg, 0.21 mmol) in MeCN (300 ml) under Ar. Vigorous stirring was continued for 24 h. The hot soln. was filtered, evaporated, and the residue chromatographed on alumina (*Merck 90*, activity II–III, MeOH/CHCl₃ 1:9). The product was crystallized by vapour diffusion from CHCl₃ and Et₂O: pale-yellow crystals (68 mg, 37%). M.p. *ca.* 214°. UV (MeCN): 315 (15600), 305 (17300), 269 (51700). IR (KBr): 940, 1725. ¹H-NMR (CDCl₃): 2.62–2.81 (*m*, 6 H); 3.15–3.25 (*m*, 4 H); 3.50–3.65 (*m*, 10 H); 3.73 (*t, J* ≈ 10, 2 H); 4.03 (*t, J* ≈ 10, 2 H); 4.20 (*d, J* = 12.5, 2 H); 4.63 (*d, J* = 12.5, 2 H); 7.73 (*t, J* = 7.5, 2 H); 7.83 (*t, J* = 7.5, 2 H); 7.99 (*d, J* = 8.0, 2 H); 8.17 (*s*, 2 H); 8.36 (*d, J* = 8.0, 2 H). FAB-MS (pos. mode): 598 ([*M* + Na + H]⁺), 582 ([*M* + Li + H]⁺). Anal. calc. for C₃₂H₃₈N₄O₆·LiBr·H₂O (679.53): C 56.56, H 5.93, N 8.24; found: C 56.21, H 5.96, N 7.78. Some cation exchange might have occurred on chromatography (see also [3]) so that the final complex may contain Na⁺ ions.

{1,1'-[N,N':N,N'-Bis(3,6-dioxaoctamethylene)bis(aminomethyl)]-3,3'-biisoquinoline 2,2'-Dioxide}europium(III), Perchlorate ([Eu³⁺ ⊂ **1**]3ClO₄⁻). To a soln. of [Li⁺ ⊂ **1**]Br⁻ (132.2 mg, 0.2 mmol) in MeCN (1 ml) at 80°, a soln. of Eu(ClO₄)₃ (182 mg, 0.4 mmol) in MeCN (2 ml) containing ethyl orthoformate (1 ml) was added. Heating was maintained for 30 min. Pale-yellow crystals deposited soon on cooling and appeared to be pure product. The sample was left for crystallization for 5 h at r.t., filtered, washed with MeCN (5 ml), and dried *in vacuo* over P₂O₅: 184 mg (90%) of [Eu³⁺ ⊂ **1**]3ClO₄⁻. UV (MeCN): 352 (9500), 338 (8300), 267 (126000), 227 (50000). Luminescence spectrum (MeCN): λ_exc. = 337, λ_em. = 579, 589, 598, 611, 618, 682; lifetime 640 ± 20 µs; quantum yield 4%. ¹H-NMR (CD₃CN): br. signals (relative area) at −18.8(2), −12.7(2), −12.4(1), −9.9(2), −6.4(2), −3.7(2), +11.2(2), +11.8(2), +12.8(2). FAB-MS (pos. mode): 925 ([ligand, Eu, 2 ClO₄]⁺), 826 ([ligand, Eu, ClO₄]⁺). Anal. calc. for C₃₂H₃₈N₄O₆·Eu(ClO₄)₃ (1024.98): C 37.50, H 3.74, N 5.46; found: C 37.69, H 3.74, N 5.47.

[Bis(1,1'-Dimethyl-3,3'-biisoquinoline 2,2'-Dioxide)]europium(III) Chloride ([Eu(**2**)₂Cl₃]). Compound **2** (367.8 mg, 1.16 mmol) was suspended in MeCN (20 ml) and heated to 80° with stirring. EuCl₃·6 H₂O (142.0 mg, 0.38 mmol) in MeOH (1 ml) was added to the suspension together with triethyl orthoformate (5 ml). Stirring at 80° was maintained for 3 h. Evaporation yielded white microcrystalline product which was washed with Et₂O and recrystallized from MeCN. Yield 82%. M.p. 259–60° (dec.). UV (MeCN): 342 (5200), 329 (6400), 310 (21400), 298 (29500). Luminescence spectrum (MeCN): λ_exc. = 340, λ_em. = 592, 618, 700; lifetime 650 ± 10 µs; quantum yield 25%; [Eu(**2**)₂Cl₃] was taken as a standard for quantum-yield determination of the [Eu³⁺ ⊂ **1**]3ClO₄⁻ emission. Anal. calc. for C₄₀H₃₂N₄O₄·EuCl₃·2 H₂O (927.06): C 51.80, H 3.91, N 6.04; found: C 51.28, H 3.87, N 5.90.

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