Synthesis and Photochemical Properties of Luminescent Eu(III) Complexes with Macrocyclic and Macropolycyclic Ligands Incorporating 3,3′-Biisoquinoline-2,2-dioxide Units

MAREK PIETRASZKIEWICZ,* JERZY KARPIUK,
RAFAŁ GASIOROWSKI and ASHOK KUMAR ROUT
Institute of Physical Chemistry, Polish Academy of Sciences, 01-224 Warsaw, Kasprzaka, 44/52, Poland.

Abstract. Three novel ligands incorporating two, or three 3,3′-biisoquinoline-2,2′-dioxide units have been synthesized using modified standard methods of cyclization. These ligands formed photoactive mononuclear complexes with a Eu(III) cation. The ligand with two photoactive units displayed a better quantum yield for the Eu(III) emission (0.064) upon UV excitation than the other two complexes incorporating three units, whose luminescence quantum yields have been estimated to be below 0.01. The luminescence of the Eu(III) complex with two sensitizing units was not stable in aqueous solution, whereas with the two other complexes, their luminescence in solution remained for a couple of days.

1. Introduction

Photoactive lanthanide complexes have attracted a lot of attention due to their outstanding potential in applications such as luminescent markers for modern medical diagnostics based on monoclonal antibodies. Time-resolved spectrofluorimetric methods based on the lanthanide chelate-labelled monoclonals provide an exceptional sensitivity for detection of particular antigens [1].

Bicylic ligands incorporating heterocyclic units as sensitizers for the Eu(III) emission upon UV excitation were of particular interest because of their expected strong binding of the lanthanide cations due to the macrobicyclic effect. Earlier work by Lehn and coworkers indicated a range of interesting photoactive features of the macrobicyclic lanthanide complexes, incorporating 2,2′-bipyridine, 1,10-phenanthroline and 3,3′-biisoquinoline, as sensitizing units for the lanthanide emission [2]. These photochemical supramolecular devices work according to the absorption energy transfer-emission process [3].

---

* Author for correspondence.

Although the nitrogen-containing heterobiaryls are not particularly strongly binding ligands for lanthanide ions, their cooperative effect in the cryptand framework makes the whole ligand a relatively efficient receptor for encapsulation of the lanthanide cation. It should be noted, however, that the corresponding bis-N-oxides of heterobiaryls are much better ligands for lanthanide complexation, and at the same time much better sensitizers for lanthanide emission. Earlier works by Italian groups reported excellent luminescent properties of the lanthanide complexes with N-oxide ligands [4]. A few papers have appeared to date dealing with macrocyclic, or macrobicylic ligands bearing heterocyclic N-oxides [5]. Of particular interest to us was the use of 3,3'-biisoquinoline-2,2'-dioxide as a sensitizing unit [5b]. Its 2 : 1 complex with europium chloride displayed outstanding emission properties upon UV irradiation, for which the quantum yield for Eu(III) emission was found to be 0.25. It was reasonable to suppose that the introduction of several sensitizing units should result in a better quantum yield for the lanthanide emission, as a result of an enhanced 'antenna effect' [6].

We now wish to report on the synthesis and photophysical properties of macro-monocyclic and macropolycyclic europium(III) complexes incorporating 3,3'-biiso-quinoline-2,2'-dioxide units.

2. Experimental

2.1. MATERIALS AND METHODS

All chemicals were purchased from Merck or Aldrich, and used as received, except MeCN and DMF which were distilled over calcium hydride under Ar prior to the synthesis of the ligands. Na_2CO_3 was finely ground and dried at 250 °C, and CF_3SO_3Na was dried at 100 °C over P_2O_5. ^{1}H NMR spectra were recorded on a Varian-Gemini 200 MHz spectrometer; IR spectra on a Beckman spectrometer, UV spectra on a CARY 1E spectrometer, and mass spectra on an Intectra AMD-604 spectrometer. The fluorescence spectra of undeoxygenated MeCN solutions were recorded on a spectrofluorimeter constructed by Jasny [7]. The samples were excited at 330 nm. Luminescence lifetimes and quantum yields for Eu(III) emission were measured as in Ref. [5b]. Elemental analyses were performed by the Microanalysis Service at the Institute of Organic Chemistry of the Polish Academy of Sciences. The melting points could not be observed – all compounds decomposed before reaching melting point.

2.2. SYNTHESIS

2.2.1. *Synthesis of the Monocyclic Ligand* **1** *Comprising Two 3,3'-Biisoquinoline-2,2'-dioxide Units*

Lithium p-toluenesulfonamide (708 mg, 4 mmol) and 1,1'-bis(bromomethyl)-3,3'-biisoquinoline-2,2'-dioxide [5b] (948 mg, 2 mmol) were suspended in dry DMF

(50 mL) and stirred at ambient temperature for 96 hr. Water was added (80 mL) and the precipitate was filtered off, washed with water, and dried *in vacuo*. The crude product was chromatographed on silica (Merck 60, 230–40 mesh, 20% MeOH in methylene chloride, v/v as eluent). Yield 106 mg, 11%.

2.2.2. *Synthesis of the Macrobicyclic Ligand **2** Incorporating Three 3,3′-Biisoquinoline-2,2′-Dioxide Units*

A mixture of 1,1′-bis(bromomethyl)-3,3′-biisoquinoline-2,2′-dioxide (1.429 g, 3 mmol), Na_2CO_3 (3.2 g, 30 mmol), CF_3SO_3Na (0.258 g, 1.5 mmol), and NH_4HCO_3 (0.158 g, 2 mmol) in MeCN (500 mL) was heated at 90 °C with vigorous stirring under Ar for 24 h in a medium-pressure glass reactor. The solution was filtered off while hot, and the inorganics were washed with MeCN. After evaporation the residue was chromatographed on silica (Merck 60, 230–400 mesh) with 10% and 20% MeOH in CH_2Cl_2. Two fractions were obtained: '**A**' and '**B**'. The total yield for both compounds as sodium complexes was 0.479 g (41%). The composition of **A**/**B** was 42 : 58, as estimated by analytical HPLC.

2.2.3. *Synthesis of Macropolycyclic Ligand **3** Incorporating Three 3,3′-Biisoquinoline-2,2′-Dioxide Units*

A mixture of 1,1-bis(bromomethyl)-3,3′-biisoquinoline-2,2′-dioxide (1.429 g, 3 mmol), 1,4,7-triazacyclononane (0.258 g, 2 mmol), Na_2CO_3 (3.1 g, 30 mmol) and CF_3SO_3Na (0.52 g, 3 mmol) were placed in a medium-pressure glass reactor containing MeCN (500 mL). Vigorous stirring was maintained for 24 h at 90 °C under Ar. The inorganic solids were filtered off while hot, and the filtrate was evaporated. The residue was chromatographed on alumina (Merck 90, II, III activ., CH_2Cl_2-MeOH 95 : 5 as eluent). Yield 0.69 g (43%) as sodium complex. Two possible configurational isomers due to axial chirality of the 3,3′-biisoquinoline-2,2′-dioxide unit could not be separated, as in the case of **2**(**A**/**B**).

2.2.4. *Eu(III) Complex Preparation with Ligand **1***

Ligand **1** (48 mg, 0.05 mmol) was added to a hot solution of europium perchlorate (22.5 mg, 0.05 mmol) in MeCN (2 mL). After cooling the product was crystallized by vapour diffusion with ethyl ether. Yield 63 mg (90%).

2.2.5. *Eu(III) Complex Preparation with the Ligands **2***

The Eu(III) complexes of **2A** and **2B** were prepared by treatment of both Na^+ complexes with europium trifluromethanesulfonate in MeCN solution. The yields were 31% for Eu(III) : **2A** and 63% for Eu(III) : **2B**.

Table I. Analytical data for the ligands **1–3** and their Eu(III) complexes.

Ligand	
1	IR (KBr, cm^{-1}), ν = 1160, 1300, 1340. ^{1}H-NMR(CF$_3$COOH, TMS ppm) δ = 8.99 and 8.20–7.59 (m, 28H, arom.); 6.00–4.90 (bm, 8H, CH$_2$N); 2.53 (s, 6H, 2 × CH$_3$). MS (8 eV), m/z = 989 (M$^+$ + Na$^+$, 100%), 967 (M + H$^+$). *Anal. Calc.* for C$_{54}$H$_{42}$N$_6$O$_8$S$_2$: C, 67.06; H, 4.38; N, 8.69; *found* C, 66.97; H, 4.33; N, 8.72.
Eu(III) : 1	IR (KBr, cm^{-1}), ν = 1120, 1150. UV(MeCN, nm), $\lambda(\epsilon)$ = 235 (102 000), 263 (140 000), 303 (25 000), 332 (11 000), 346 (8300). MS (8 eV), m/z = 1317 (M ClO$_4^-$, 100%), 1284, 1218, 1119. Flourescence (MeCN, λ_{exc} = 330 nm, nm), λ_{cm} = 580, 590, 595, 614, 618, 650, 693; lifetime: 0.25 ms; quantum yield: 0.064. *Anal. Calc.* for C$_{54}$H$_{42}$Cl$_3$N$_6$O$_8$S$_2$Eu: C, 52.94; H, 3.46; N, 6.86; *found* C, 52.71; H, 3.37; N, 6.72.
2A : Na$^+$	IR (KBr, cm^{-1}) ν = 1578, 1570, 1382, 1260 (N—O). ^{1}H-NMR (DMSO-d_6, TMS, ppm) δ = 8.6–7.7, (m, 30H, aromat.), 4.8 and 4.2, (2d, 6 × CH$_2$) MS (SIMS), m/z = 994 (M + Na$^+$), 1009 (M + K$^+$). *Anal. calc.* for C$_{60}$H$_{42}$N$_8$O$_6$·NaSO$_3$CF$_3$· 2H$_2$O·CH$_2$Cl$_2$: C, 58.94; H, 3.83; N, 8.88; *found* C, 58.77; H, 3.79; N, 8.73.
2B : Na$^+$	IR (KBr, cm^{-1}) ν = 1580, 1575, 1382, 1260 (N—O). MS(SIMS), m/z = 994 (M + Na$^+$, 100%) 1009 (M + K$^+$). *Anal. calc.* for C$_{60}$H$_{42}$N$_8$O$_6$· NaSO$_3$CF$_3$·2H$_2$O·CH$_2$Cl$_2$: C, 58.94; H, 3.83; N, 8.88; *found* C, 58.84; H, 3.71; N, 8.78.
2A : Eu^{3+}	IR (KBr, cm^{-1}) ν = 1580, 1575, 1255 (N—O). Fluorescence (MeCN, λ_{exc} = 330 nm, nm): 579, 613, 652, quantum yield: 0.0022; lifetime: 0.25 ms. *Anal. calc.* for C$_{60}$H$_{42}$N$_8$O$_6$·Eu(SO$_3$CF$_3$)$_3$·2H$_2$O: C, 47.07; H, 2.89; N, 6.97; *found* C, 47.02; H, 2.71; N, 6.92.
2B : Eu^{3+}	IR (KBr, cm^{-1}) ν = 1580, 1570, 1255 (N—O). Fluorescence (MeCN, λ_{exc} = 330 nm, nm): 579, 613, 652; quantum yield: 0.0015; lifetime: 0.24 ms. *Anal. calc.* for C$_{60}$H$_{42}$N$_8$O$_6$· Eu(SO$_3$CF$_3$)$_3$·2H$_2$O: C, 47.07; H, 2.89; N, 6.97; *found* C, 46.97; H, 2.59; N, 6.91.
3 : Na$^+$	IR (KBr, cm^{-1}) ν = 1580, 1390, 1260 (N—O). ^{1}H-NMR (CDCl$_3$, TMS, ppm) δ = 8.8–7.5, (m, 30H, aromat.); 4.5, (bm, 12H, 6 × CH$_2$Ar); 3.7–3.1, (m, 24H, NCH$_2$–CH$_2$N). MS (SIMS), m/z = 1217 (M + Na$^+$). *Anal. calc.* for C$_{72}$H$_{66}$O$_6$N$_{12}$·NaSO$_3$CF$_3$·H$_2$O: C, 63.59; H, 4.91; N, 12.03; *found* C, 63.11; H, 4.81; N, 12.11.
3 : Eu^{3+}	IR (KBr, cm^{-1}) ν = 1578, 1570, 1262 (N—O). Fluorescence (MeCN, λ_{exc} = 330 nm, nm): 594, 616, 653, 703; quantum yield: 0.001; lifetime: 0.14 ms. *Anal calc.* for C$_{72}$H$_{66}$O$_6$N$_{12}$·Eu(CF$_3$SO$_3$)$_3$·H$_2$O: C 53.03; H 4.04; N 9.90; *found:* C 5289; H 3.96; N 9.86

2.2.6. *Eu(III) Complex Preparation with Ligand* **3**

The sodium complex of the ligand **3** (0.069 g, 0.05 mmol) was suspended in MeCN (5 mL) and heated to 60 °C with stirring. Europium trifluoromethanesulfonate (0.030 g, 0.05 mmol) was added to the suspension. A clear solution was formed instantly, and left for crystallization by vapour diffusion with ethyl ether. Yield 0.075 g, 84%.

Analytical data for all ligands **1–3** and their complexes are presented in Table I.
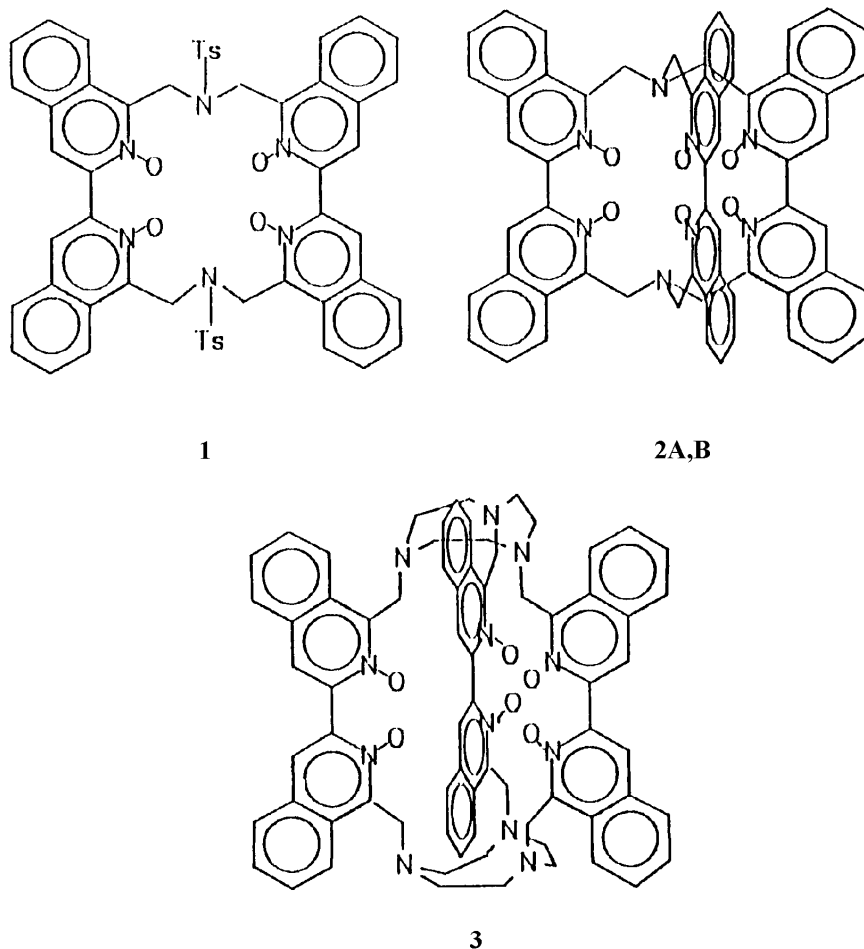
Figure 1. The structural formulas of the ligands incorporating 3,3′-biisoquinoline-2,2′-dioxide units.

3. Results and Discussion

All new ligands prepared are shown in Figure 1.

The macromonocyclic ligand **1** turned out to be very poorly soluble in most organic solvents, thus this accounted for a low yield and remarkable difficulties in NMR characterization. Its complex with europium perchlorate was prepared by mixing equimolar amounts of the ligand and europium salt in acetonitrile at 60 °C. Partial evaporation of the solvent resulted in deposition of small pale-yellow crystals, whose FAB MS and microanalysis were consistent with 1 : 1 stoichiometry.

The fluorescence spectrum of the Eu(III) : 1 complex was recorded in MeCN solution, and consisted of several lines corresponding to the transitions shown in Table II.

Table II. Eu(III) transitions from the $^5D_0$ level.

λ_{em} (nm)	Transition
580	$^5D_0 \Rightarrow {}^7F_0$
590, 595	$^5D_0 \Rightarrow {}^7F_1$
614, 618	$^5D_0 \Rightarrow {}^7F_2$
650	$^5D_0 \Rightarrow {}^7F_3$
693, 700	$^5D_0 \Rightarrow {}^7F_4$

The emission at 614 nm was the most prominent. The quantum yield for the Eu(III) emission was estimated to be 0.064 (experimental error $\pm 30\%$) and the luminescence lifetime 0.25 ms. The complex was not stable in aqueous solution. A total loss of fluorescence was observed upon addition of water (H_2O–MeCN, $1:1$) after 2 h. Although the new complex showed excellent luminescent properties, its potential application as a fluorescent label for medical diagnostics is limited, due to a total loss of fluorescence in aqueous solution.

We have used a slightly modified synthetic procedure for the single-step synthesis of macrobicyclic ligands incorporating the same three units [2a]. Ammonia was replaced by ammonium hydrogen carbonate, and sodium trifluoromethanesulfonate was used as a template. A one-pot, sodium ion-promoted macrobicyclization was achieved, starting from 1,1′-bis(bromomethyl)-3,3′-biisoquinoline-2,2′-dioxide, ammonium hydrogen carbonate, sodium trifluoromethanesulfonate and powdered sodium carbonate, in a medium-pressure glass reactor, at 80 °C in acetonitrile. It is noteworthy that sodium bromide as a templating agent proved to be totally ineffective. The final product was isolated in 41% yield by chromatography on silica. Because of restricted rotation about the single bond linking the two isoquinoline units, the final bicylic product may exist in two diastereoisomeric forms. One isomer consists of three biisoquinoline units of the same configuration, whereas the second isomer differs in an opposite axial configuration of one biisoquinoline unit. We have assigned these isomers as **2A** and **2B**. Both compounds were isolated by chromatography as their sodium complexes, but it was impossible to obtain suitable crystals for X-ray analysis to distinguish their axial configuration. It was possible to exchange sodium for europium(III) cation by a simple exchange with europium trifluoromethanesulfonate in MeCN solution at elevated temperature. The fluorescence spectra of the Eu(III) complexes of **2A** and **2B** were recorded in acetonitrile solution at room temperature. The shapes of both spectra are very similar (Figure 2).

The fluorescence spectrum of the **2A** : Eu(III) complex consists of several bands at 579, 613 (the most prominent) and 652 nm, when excited at 330 nm. The quantum yield was estimated to be 0.0022 in MeCN and the luminescence lifetime was 0.25 ms. The fluorescence spectrum of the **2b** : Eu(III) complex displayed similar bands
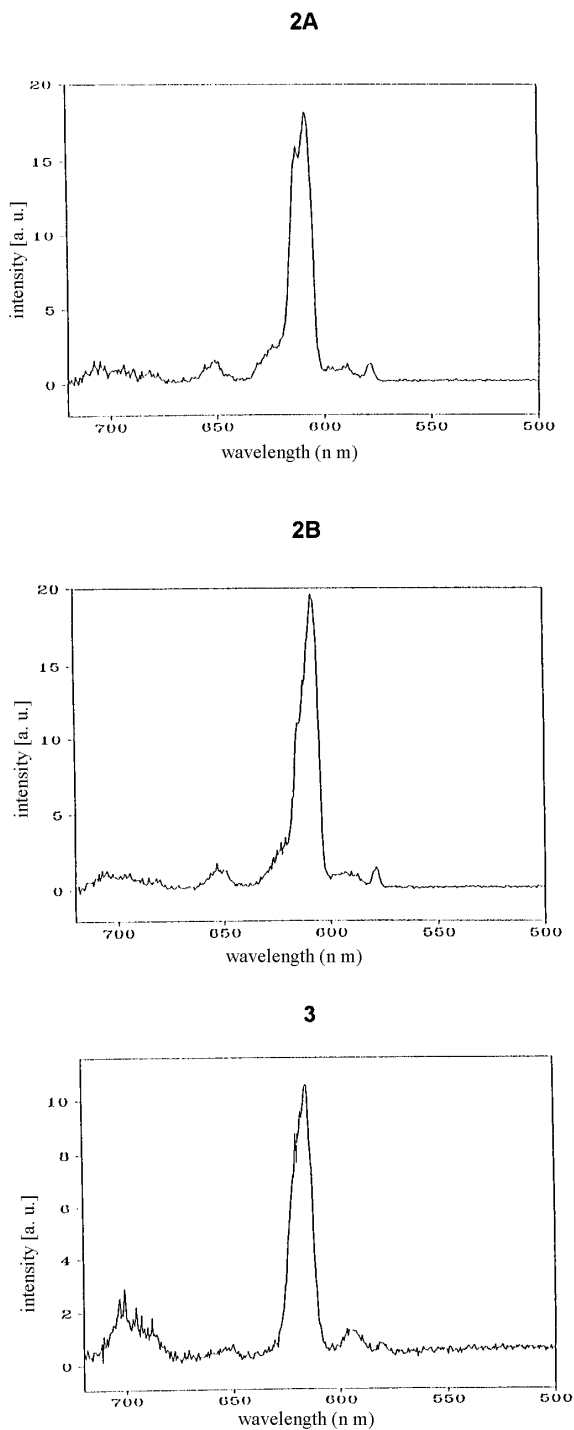
2A

2B

3

Figure 2. Corrected fluorescence spectra of the Eu(III) complexes of **2A**, **2B** and **3**.

at 579, 608 (the most prominent), and 652 nm. The quantum yield was 0.0015, and the luminescence lifetime was 0.24 ms.

We expected to observe an enhanced fluorescence of these complexes incorporating three biisoquinoline units, due to their collective light harvesting ('antenna effect'). Our earlier studies on the bicyclic ligand based on 1,10-diaza-18-crown-6 and one biisoquinoline unit linking nitrogen atoms and its Eu(III) complex [5b] revealed the quantum yield of Eu(III) emission to be 0.04. In the present study both complexes with **2A** and **2B** are less efficient as light-converting devices. This fact may be interpreted by proposing that the three-dimensional cavity of **2A** and **2B** is remarkably tight and encapsulation of the Eu(III) cation must be associated with considerable distortion of the biisoquinoline units. This implies that the dihedral angle between isoquinoline-N-oxide units may be quite large and the energy transfer from the distorted biisoquinoline unit may not be so efficient. On the other hand, the spectra are very similar, suggesting an almost equal coordination pattern around the Eu(III) cation. As postulated earlier, the two isomers should differ markedly because of their differences in axial chirality. Thus the emission pattern for both complexes was expected to be very different, since lanthanide emission is very sensitive in respect of small coordinational changes. These striking similarities in their fluorescence spectra may be interpreted by proposing that the Eu(III) cation forms in both cases *exclusive* rather than *inclusive* complexes. The *exclusive* complex would also account for a low quantum yield for the emission, since the cation would be exposed to the influence of the solution environment, particularly residual water which quenches the fluorescence.

In order to make more room for the cation in the cavity, the cylindrical, polycyclic ligand **3** was devised. Again, three photoactive units were thought to be connected by two small macrocyclic caps: 1,4,7-triazacyclononane.

A '2 + 3' condensation of 1,4,7-triazacyclononane with 1,1′-bis(bromomethyl)-3,3′- biisoquinoline-2,2′-dioxide in MeCN and in the presence of sodium trifluoromethanesulfonate as a template led to the desired compound **3** in 43% yield after purification by chromatography. It is remarkable that this reaction proceeded in one step, where six C—N bonds were formed. We noted also a dramatic influence of the counterion of the template agent in this condensation. Initial use of sodium bromide as a templating agent led to a polymeric material only.

Ligand **3** readily formed the mononuclear complex with europium trifluoromethanesulfonate in MeCN solution in 84% yield. The fluorescence spectrum of the Eu(III) complex was recorded in acetonitrile solution at ambient temperature, and displayed several bands at 594, 616 (the most intense), 653, 703 nm. The luminescence quantum yield was estimated to be 0.001, and the lifetime 0.14 ms. It is somewhat surprising that the quantum yield of the emission process for Eu(III) was relatively low. This may be interpreted by postulating that the three-dimensional cavity is too large for the Eu(III) cation, and the cation is not tightly held in this cavity. Thus, small molecules of water may penetrate the first coordination sphere of the europium cation and may account for the remarkable

quenching of the fluorescence. Many attempts have been made to obtain crystals of all new complexes suitable for X-ray crystallographic studies, which would have a remarkable impact on the interpretation of the results. However, monocrystals good enough for structural studies could not be grown. It may probably be related to the presence of a mixture of diastereoisomers due to the axial chirality of 3,3′-biisoquinoline-2,2′-dioxide.

4. Conclusions

We have discovered a remarkable 'template effect' for the macrobicyclization and macropolycyclization promoted by sodium cation, which works only in this case when the counterion of the sodium salt is weakly coordinating. Thus we selected trifluoromethanesulfonate as the counterion. The monocyclic complex was not stable in aqueous solution, whereas bicylic, and macropolycyclic complexes were photoactive in water for several days. Our study indicated that the introduction of more light-harvesting units does not necessarily mean better performance of the lanthanide emission due to the collective effect of several photoactive sensitizing units. It is very likely that a better fit of the coordinating units around the lanthanide cation may effect better energy transfer from the sensitizing units to the lanthanide ion. It would be worthwhile to investigate a ligand of 'tripod' architecture where the coordinating units would have much more flexibility to wrap around the lanthanide ion according to its coordination pattern. Our future work will include less rigid ligands capable of adopting conformations more suitable for the coordination geometry of the lanthanide ion, than in the case of rigid, macrobicyclic, or macropolycyclic ligands.

Acknowledgement

References

1. E. Soini and T. Lövgren: *CRC Critical Rev. Anal. Chem.* **18**, 105 (1987).
2. (a) J.-C. Rodriguez-Ubis, B. Alpha, D. Plancherel and J.-M. Lehn: *Helv. Chim. Acta*, **67**, 2264 (1984); (b) A. Caron, J. Guilhem, C. Riche, C. Pascard, B. Alpha, J.-M. Lehn and J.-C. Rodriguez-Ubis: *Helv. Chim. Acta*, **68**, 1577 (1985); (c) B. Alpha, J.-M. Lehn and G. Mathis: *Angew. Chem. Int. Ed. Engl.* **26**, 266 (1987); (d) B. Alpha, V. Balzani, J.-M. Lehn, S. Perathoner and N. Sabbatini: *Angew. Chem. Int. Ed. Engl.* **26**, 1266 (1987); (e) N. Sabbatini, S. Perathoner, V. Balzani, B. Alpha and J.-M. Lehn: *Supramolecular Photochemistry*, V. Balzani (Ed.), Reidel, Dordrecht, Boston, Lancaster, Tokyo, p. 187 (1987); (f) B. Alpha, E. Anklam, R. Deschenaux, J.-M. Lehn and M. Pietraszkiewicz: *Helv. Chim. Acta*, **71**, 1042 (1988); (g) V. Balzani, E. Berghmans, J.-M. Lehn, N. Sabbatini, R. Terode and R. Ziessel: *Helv. Chim. Acta*, **73**, 2083 (1990); (h) V. Balzani, J.-M. Lehn, J. van de Loosdrecht, A. Mecati, N. Sabbatini and R. Ziessel: *Angew. Chem. Int. Ed. Engl.* **30**, 190 (1991).
3. W. De W. Horrocks and M. Albin: *Progr. Inorg. Chem.* S.J. Lippard (Ed.), Vol. 31, John Wiley & Sons, New York, Chichester, Brisbane, Toronto, Singapore, p. 1 (1984).

4. A. Musumeci, R.P. Bonomo, V. Cucinotta and A. Seminara: *Inorg. Chim. Acta*, **59**, 133 (1982);
    (c) A. Seminara and E. Rizzarelli: *Inorg. Chim. Acta*, **40**, 249 (1980); (c) A. Seminara and A.
    Musumeci: *Inorg. Chim. Acta*, **95**, 291 (1984).

5. (a) M. Pietraszkiewicz, S. Pappalardo, P. Finocchiaro, A. Mamo and J. Karpiuk: *J. Chem. Soc.,
    Chem. Commun.* 1907 (1989); (b) J.-M. Lehn, M. Pietraszkiewicz and J. Karpiuk: *Helv. Chim.
    Acta*, **73**, 106 (1990); (c) S. Pappalardo, F. Bottino, L. Giunta, M. Pietraszkiewicz and J. Karpiuk:
    J. Incl. Phenom. **10**, 387 (1991); (d) J.-M. Lehn and C. O. Roth: *Helv. Chim. Acta*, **74**, 572 (1991);
    (e) L. Prodi, M. Maestri, V. Balzani, J.-M. Lehn and C.O. Roth: *Chem. Phys. Lett.* **180**, 45 (1991);
    (f) M. Pietraszkiewicz, J. Karpiuk and A.K. Rout: *Pure Appl. Chem.* **65**, 563 (1993).

6. B. Alpha, R. Ballardini, V. Balzani, J.-M. Lehn, S. Perathoner and N. Sabbatini: *Photochem.
    Photobiol.* **52**, 299 (1990).

7. J. Jasny, *J. Luminescence* **17**, 149 (1978).