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MOLECULAR DYNAMICS STUDY OF THE COMPLEXATION OF LUMINESCENT CATIONS BY ENCAPSULATING LIGANDS WITH BIPYRIDINE UNITS

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Based on MD simulations, the structures of Eu^{3+} and $EuCl_3$ complexes of bipyridine-substituted calixarenes in different environments (*in vacuo* and in acetonitrile and water solutions) were modelled. The data account for the differences in their luminescence properties. The role of the calixarene platform, preorganization of the ligands, and an explicit account of counterions in different environments are analysed. © 1997 by John Wiley & Sons, Ltd.

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INTRODUCTION

The search for synthetic ligands able to complex metal ions has played a central role in supramolecular chemistry and in related theoretical investigations. Indeed, in the late 1960s, when the first experimental studies on crown ether and cryptand complexes were carried out, quantum chemists introduced the 'supermolecule approach' to calculate the interaction energy between small ions and molecules mimicking the binding sites of ionophores.[1] Based on energy component analysis,[2–4] this energy was dissected into components such as electrostatic, charge transfer and polarization. The many studies on alkali metal cation complexes allowed a detailed analysis of the energy and structural basis of their recognition in the gas phase and in solution.[5]

The trivalent M^{3+} lanthanide cations also display essentially non-covalent and non-directional coordination to the surrounding ligands, because their f^n electrons are shielded by outer filled s and p orbitals. Compared with conventional ligand transition metal complexes, their complexes display versatile coordination numbers mostly controlled by steric interactions in their first coordination sphere. In this paper, we focus on structural features on a series of M^{3+} complexes involving bipyridine ligands as putative binding sites, in relation to their luminescence properties.

Their luminescence involves a light conversion process starting with light absorption by a metal ligand, followed by energy transfer to the metal ion which is the light emitter ('antenna effect').[6, 7] Significant luminescence requires the formation of a relatively stable complex and in chromophoric groups efficient in promoting the 'antenna effect,' in their spatial proximity to the complexed cation, in the controlled degree of cation shielding from the solvent molecules, involving possible counterion effects. For instance, cryptand-type ligands containing 2,2′-bipyridine combine the shielding effect upon complexation and the sensitizer 'antenna' moiety of the bipyridine groups.[8–10] Crystal structures of these Eu^{3+} and Tb^{3+} cryptates are consistent with the 'antenna effect:'[11] the cation is encapsulated inside the cavity of ligand, and makes short contacts (from 2·55 to 2·90 Å) with the eight $N_{pyridine}$ atoms. Its coordination sphere is completed by two Cl^- anions, or by one Cl^- and one H_2O molecule. This is consistent with photophysical studies in aqueous solution which indicate that Eu^{3+} remains in average accessible to about 2·5 H_2O molecules.[12]

Functionalized calixarenes can also complex luminescent trivalent cations. For instance, sensitizer-modified calix[4]arenes have been studied and the quantum yield significantly improved when the calixarene skeleton was functionalized at the upper rim with phenyl groups.[13] Calixarene derivatives with three carboxylic esters or three acid groups and one aromatic sensitizer group such as triphenylene allow for the excitation of both Eu^{3+} and Tb^{3+} at long wavelengths.[14]

In the present work we focused on calix[4]arenes functionalized by 2,2′-bipyridine units (Figure 1). Two

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extreme examples are represented by LIGI and LIGII (Figure 1), which possess a similar calixarene platform in the cone conformation and four bipyridines, attached at the 5,5′- and 6,6′-positions, respectively. The upper rim of LIGI is substituted by four *tert*-butyl groups, whereas that of LIGII is unsubstituted, but these groups are remote from the bipyridine potential binding sites and are therefore expected to have minor effect on the luminescence properties.

Although the unsubstituted 2,2′-bypiridines are known to chelate lanthanide ions in acetonitrile solution,[15] LIGI and LIGII complexes display very different luminescence properties. The luminescence quantum yield, Φ, of the complex of LIGI with Eu^{3+} is high ($\Phi = 16\%$), whereas the corresponding value for LIGII is very low ($\Phi < 1\%$).[16] On the other hand, for LIGIV (Figure 1), which differs from LIGI by one additional calix[4]arene platform, no luminescence could be observed.[17] It is not clear whether this is due to the instability of this complex or to other reasons. The

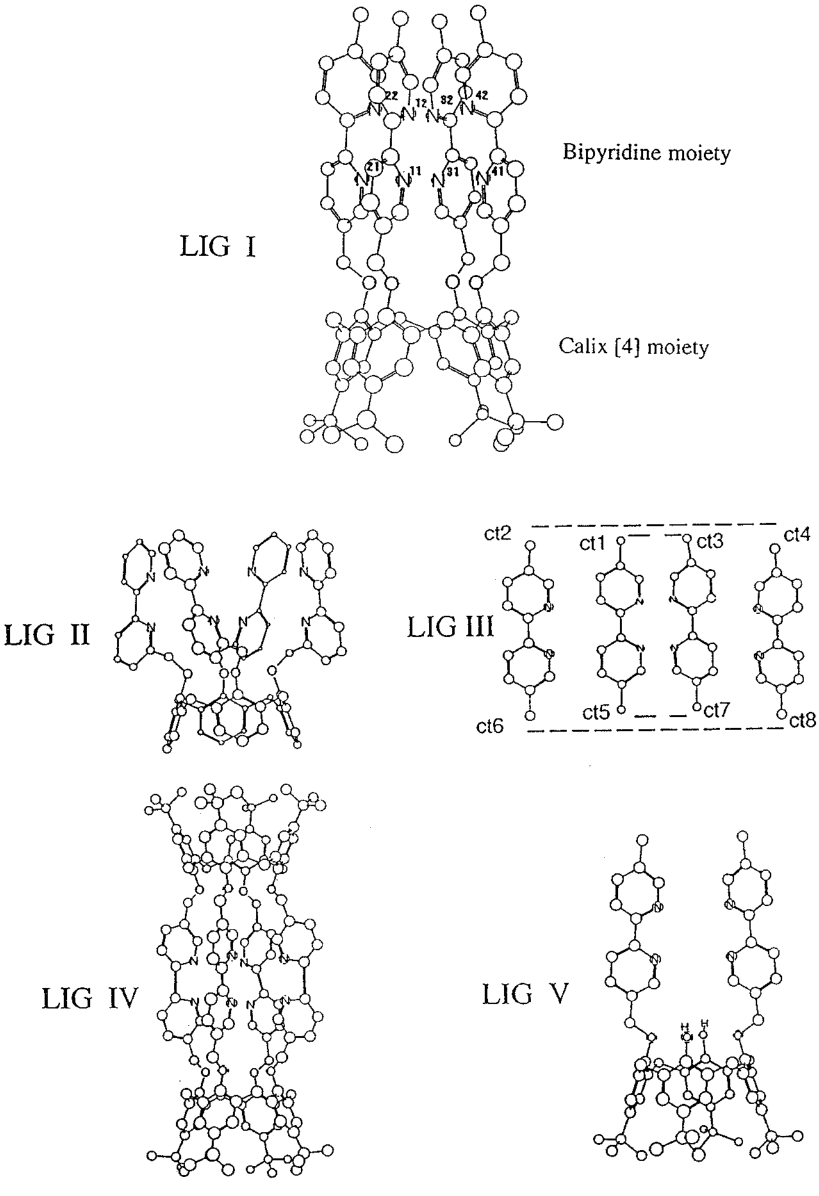

Figure 1. Ligands LIGI–LIGIV with atomic symbols used in tables

lack of x-ray structure data on these lanthanide complexes was the impetus for this study.

Computer modelling can contribute to elucidating the structure of the complex. Molecular mechanics studies in the gas phase have been reported on lanthanide complexes with macrocylic ligands.[18] Solvation, however, plays a major role in the conformation of the free ligands and in the structure and nature of the complexes. It can be accounted for by molecular dynamics simulations.[19] Following the first studies in aqueous solutions, non-aqueous solvents such as methanol, acetonitrile and chloroform have been considered. As far as M^{3+} ion complexes are concerned, early studies in water have been reported with aminopolycarboxylate ligands.[20] Other simulations on the Eu^{3+} 222 cryptate in water[21] and in acetonitrile[22, 23] showed that the complexed cation is not fully shielded by the ligand, but coordinated to about four solvent molecules, in agreement with experiment. The calculated coordination number for the free Eu^{3+} cation[21] was also in agreement with experiment. Simulations on free lanthanide(III) cations[24–26] or their LCl_3 salts[27] in pure water have been reported. The role of counterions in complexes was studied computationally with a comparison of the $EuCl_3$ and EuF_3 222 cryptates in water and acetonitrile.[28] The nature of the uncomplexed ion pairs was shown also to be very solvent dependent. With *p-tert*-butylcalix[4]arene-tetraamide as ligand, the Eu^{3+} complex was calculated to be stable in acetonitrile but not in water.[23, 29] It was stressed that counterions, not considered in the calculations, play an important role in the nature and stability of the complexes. Following these studies, van Veggel[30] simulated Eu^{3+} complexes of calix[4]arene derivatives and a bislariat diazacrown ether in methanol. His results were consistent with the experimental luminescence data.

Here, we report calculations on ligands LIGI–LIGV free and complexed with $EuCl_3$ in different environments (*in vacuo* and in acetonitrile and water), with and without Cl^- counterions, in order to investigate the relationship between their structural and luminescence properties. Although luminescence data have been reported for ligands LIGI and LIGII only, we modelled the related LIGIII–V ligands for the purpose of comparison. LIGIII, an assembly of four independent bipyridine units, is referred to in the following as a ‘ligand’ for consistency and simplicity.

We first consider the free ligands *in vacuo* and immersed in a bath of explicit acetonitrile molecules to address the question of their preorganization, i.e. to what extent they remain conformationally close to the complexed molecules. In preorganized forms, the bipyridine arms should be more or less parallel to the C_4 symmetry axis of the calixarene framework, and adopt a converging orientation of the $N_{pyridine}$ atoms (*cis* bipyridines). Two extreme situations in terms of preorganization are represented by LIGIII and LIGIV. The former lacks any anchoring platform to hold together the four bipyridines whereas in the latter two calixarene platforms maintain the bipyridine arms together, delineating a pseudo-cavity.

We then focus on the complexes with Eu^{3+} and $EuCl_3$ in order to characterize the different binding modes of the ligands and to compare their encapsulating and shielding capacities. Their structures and stabilities are discussed as a function of the calixarene platform (compare the $EuCl_3$ complexes of LIGI or LIGII with LIGIII and LIGIV). Thus, the four independent bipyridines of LIGIII are free to wrap around the cation whereas LIGIV is rigidified by the two calix[4]arenes. Another question concerns the optimum number of bipyridines to be attached to the calixarene platform. This led us to simulate in acetonitrile the $EuCl_3$ complex of LIGV, with two bipyridine arms only, to be compared with the complex of LIGI.

As the Eu^{3+}–solvent attractions compete with the Eu^{3+}–ligand attractions, the solvation effect can be assessed by comparing results *in vacuo* (as a reference state) and in acetonitrile and water solutions. *In vacuo* the only hindrance for bipyridines to converge to Eu^{3+} is due to topoligical and steric constraints of the ligand. Acetonitrile is often used as a solvent in experimental studies of lanthanide complexes. Although the studied ligands are not water soluble, we decided to simulate the complexes in water because water is among the most efficient solvent competitors against cation complexation. Furthermore, in water-containing acetonitrile solution, some water molecules might coordinate the complexed Eu^{3+} ion and quench its luminescence.

Another matter of interest concerns the role of counterions in the structure and luminescence of the complexes. Experimental studies have shown that lanthanide(III) ions may form intimate ion pairs with the counterions, especially in poorly coordinating solvents.[31] The anion size, shape and polarizability may be discriminant in the balance of competing cation–anion and anion–solvent interactions. In this study, we selected Cl^- as a counterion because it is often used experimentally with lanthanide complexes.[16, 32] As shown for Eu^{3+} 222 cryptates in acetonitrile solution,[28] they compete strongly with the ligand binding to the cation. It is therefore likely that if we find no direct Cl^- coordination to Eu^{3+}, other bulkier and softer anions also would not bind.

EXPERIMENTAL

The calculations were performed with the AMBER4.0 package for MM and MD simulations[33] using the AMBER force field.[34, 35] One key feature was the non-covalent representation of the Eu^{3+} cation, as done in simulations on alkali or alkaline earth metal cation complexes in solution.[36] Although some force fields use a covalent representation of the cation–ligand binding,[37, 38] we preferred to allow for dynamic exchanges within the M^{3+} coordination sphere, as a result of the competition between the ligand, solvent molecules and counterions. The non-covalent interactions were depicted by a 1–6–12 potential, where the electrostatics are approximated by coulombic interactions without an explicit polarization term. The van der Waals ε and R^* parameters for Eu^{3+} were the same as in Ref. 23. For Cl^-,

ε and R^* were taken from Ref. 21. All atomic charges are reported in Charts SI and II (Supplementary material; available from the authors on request). Those of the bipyridine moiety were taken from previous studies on helicates,[39] which are oligobipyridine ligands forming helices around encapsulated metal ions.[40, 41] With these charges, a molecular mechanics calculation on the 2,2′-bipyridine *cis–trans* energy difference (8·6 kcal mol^{-1}) is found to be similar to the *ab initio*-calculated vlaue (7·3 kcal mol).[42] The charges on the calix[4]arene moiety were taken from Fischer *et al*.[43]

The acetonitrile and water molecules were represented with a three-point model, with OPLS[44] and TIP3P parameters, respectively, derived by Jorgensen *et al*.[45] from Monte Carlo simulations on the pure liquids. The solvents were explicitly represented by a cubic box about 30 Å in length, using periodic boundary conditions. A residue-based cut-off of 10 Å was used for non-bonded interactions.

The system was coupled to a temperature bath[46] at 300 K with a coupling constant $\tau_T = 0{\cdot}1$ ps. The equations of motion were integrated using a time step of 1 fs, starting with random velocities. The bonds with hydrogen atoms and those of solvent molecules were kept rigid using the SHAKE method.[47] After a conjugate gradient energy minimization (with a root mean square deviation on the energy of $< 0{\cdot}5$ kcal mol^{-1}), MD simulations were run first for 20 ps with the BELLY option[33] in order allow the solvent to reorganize around the solute kept rigid. This was followed by free MD simulations of 100 ps for the free ligands and for the water simulations, and of 200 ps for the complexes *in vacuo* and in acetonitrile solution.

All the starting structures were model built and minimized *in vacuo*. The Eu^{3+} ion was initially placed equidistant from the eight bipyridine nitrogen atoms. Counterions were added at a distance of 6–7 Å from Eu^{3+}, in a plane perpendicular to the C_4 symmetry axis. In all cases, structures obtained after 200 ps of MD *in vacuo* were used as starting structures for the simulations in solution. The only exception concerns the LIGII–$EuCl_3$ complex (see below). For the LIGIII–$EuCl_3$ complex, two initial locations of counterions were considered, LIGIII^{eq} with the three Cl^- ions in the ‘equatorial plane’(i.e. perpendicular to the C_4 axis), and LIGIII^{ax} with one Cl^- moved to an ‘axial’ position.

The analysis of the trajectories was performed with MDS software[48] from the trajectories which were saved every 0.2 ps.

RESULTS

In this section, we present the structures of the free ligands, followed by their $EuCl_3$ and Eu^{3+} complexes in the gas phase and in acetonitrile and water solutions. The results most relevant to the luminescence experiments concern the $EuCl_3$ complexes of LIGI and LIGII. A summary of the final coordination numbers of Eu^{3+} is given in Table 2.

Conformation of the free ligands

The simulations of the free ligands started with the conformers ‘organized’ for complexation, i.e. where the bipyridines converge to the centre of the pseudo-cavity. The structures were obtained from the gas-phase model-built Eu^{3+} complexes in which the cation was removed.

We characterize the overall conformational flexibility by the fluctuations of opposite C_t–C_t distances, of dihedral angles CA–OS–CT–CA and by the frequency of *cis–trans* interconversions. The behaviour of the ligands I–IV in the examined environments is very different. The degree of preorganization that we observe follows in general the sequence LIGIV > LIGI > LIGII > LIGIII. In the most rigid LIGIV ligand, the only noticeable motions concern frequent *cis–trans* interconversions within each bipyridine unit, and oscillations of the cone of the calixarenes, as found in related systems.[20, 29] Such motions do not seem sufficient to open the bipyridine cavity and to provide an easy path for cation inclusion therein.

The ‘bipyridine cage’ (Figure 2) of LIGI retains more or less its initial closed form in the gas phase and in acetonitrile, with only three bipyridine arms remaining *cis* and axial while the fourth one relaxes to a *trans* conformation. As the simulation time may be too short to allow conformational changes in acetonitrile, we rerun 200 ps of MD starting with an ‘open’ arrangement of the four bipyridine arms of LIGI. In acetonitrile solution the two forms have similar average intrinsic energies. However, the open form has larger interactions with the solvent than the closed one (-204 and -179 kcal mol^{-1}, respectively), and should therefore be more populated. As a result, in acetonitrile, the ligand LIGI is not preorganized as far as the precise orientation of binding sites is concerned.

LIGII cannot be preorganized either in any environment (Fig. 2). Its bipyridines cannot form a cage since, as will be discussed later, this ligand is not able to wrap around the Eu^{3+} ion. One bipyridine adopts a *trans* conformation and the ‘cage’ is more open in water than in acetonitrile. In fact, in water one arm is totally bent in a perpendicular arrangement with respect to the calixarene C_4 symmetry axis.

The four bipyridines of LIGIII, not topologically linked together, dissociate after a few ps in all the studied environments. *In vacuo*, as in acetonitrile and water, two bipyridines remain first in close proximity, but dissociate later.

In water all ligands are in general less ‘organized’ than in acetonitrile solution (Fig. 2) because the $N_{pyridine}$ atoms are attracted by water, leading to frequent *cis–trans* interconversions of the bipyridines. A second water effect is the tendency to fill the bipyridine cavity, which therefore opens. For example, in the case of LIGII, there are two water molecules within 3·5 Å of the centre of mass of the $N_{pyridine}$ atoms, whereas in acetonitrile there are no solvent molecules within 7·0 Å from the centre.

It could be expected that the formation of a cage with the

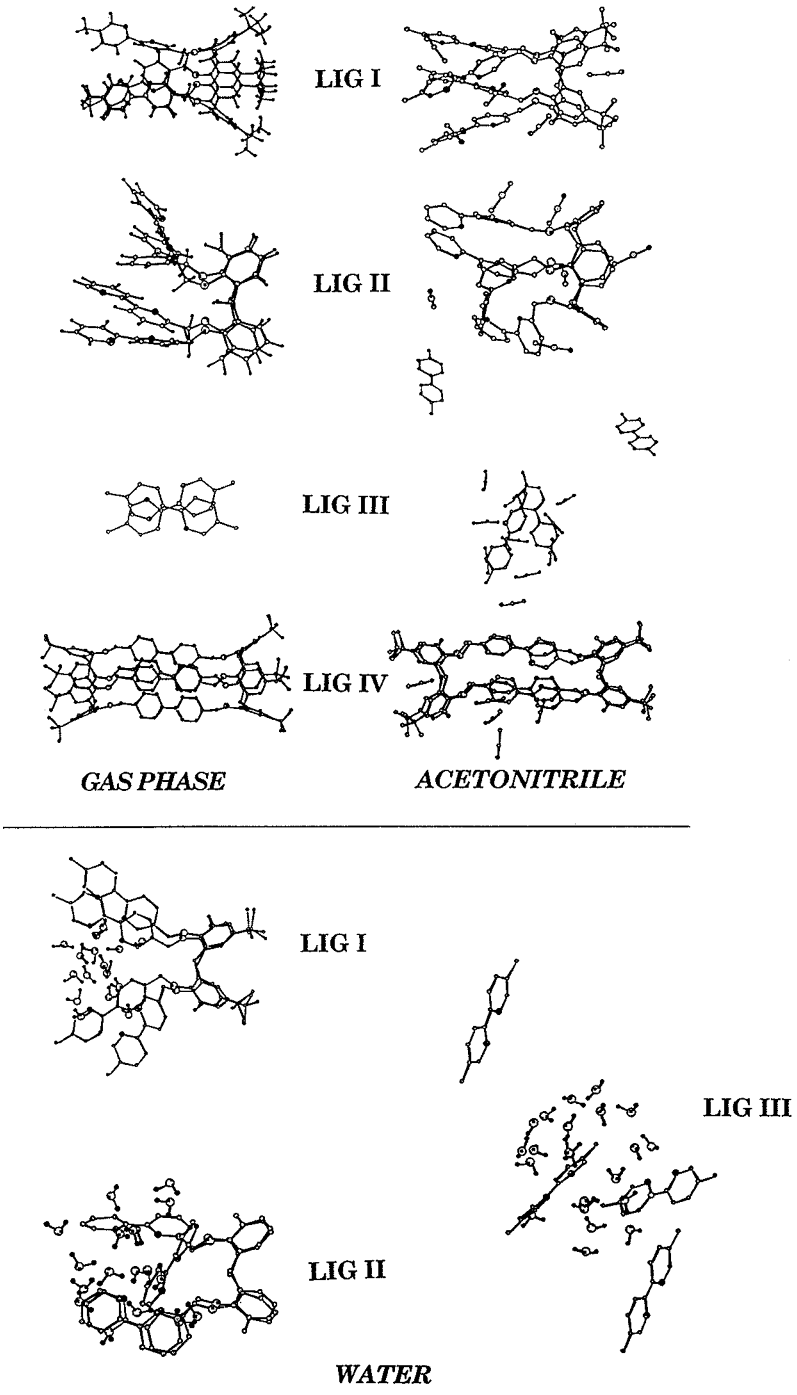

Figure 2. Free ligands. Snapshots after 120 ps of simulation in different environments

four bipyridines requires some repulsion between these ligands to be taken into account. This is not the case. Indeed, in LIGIV where this cage is most compact, the interaction energy of each bipyridine with the three others is attractive (from about -18 to -11 kcal mol^{-1} *in vacuo* and in acetonitrile; Table 1), mostly owing to the van der Waals contribution. In other compact arrangements, such as in LIGI, these values are also attractive *in vacuo* and in acetonitrile. In water, some bipyridine–bipyridine interactions become repulsive, presumably because the orientation becomes driven by the solvation of the N atoms (see LIGI and LIGIII, Figure 2 and Table1).

Thus, to summarize, the different luminescence properties of LIGI and LIGII complexes cannot be related to differences in the preorganization of the free ligands. This is why the other free ligands have not been simulated in solution.

Eu^{3+} and $EuCl_3$ complexes of calix[4]arene(bipyridine)$_4$: comparison of LIGI and LIGII

In this section, we describe the LIGI and LIGII complexes, i.e. with two hosts containing the calix[4]arene(bipyridine)$_4$ framework. We mostly focus on the modulation of the LIGI–Eu^{3+} structure as a function of the environment and of the counterions.

Typical structures are shown in Figure 3. In Table 2 we report the total coordination number CN of the complexed Eu^{3+} in the different environments. The average distances betweenEu^{3+} and the $N_{pyridine}$ and Cl^- atoms are given in Table S-III (Supplementary material). In the case of late structural changes, these average distances may differ from the final ones. In these cases, we refer to distances at the end of simulations.

Structural parameters describing the shape of the bipyridine cage for LIGI, LIGIII and LIGIV complexes with $EuCl_3$ are reported in Table S-IV (Supplementary material). In the following, in order briefly to characterize the number *n* of bipyridine 'branches' involved in the cation coordination, we refer to '*n*-branched' complexes.

LIGI complexes with Eu^{3+} and $EuCl_3$

LIGI is a good ligand for Eu^{3+} or $EuCl_3$, with different patterns depending on the environment. First, in the gas phase and in acetonitrile solution, it is clear that the four bipyridines of LIGI are able to wrap around Eu^{3+} when no counterions compete with the ligand, with eight Eu^{3+}–N short distances (from 2·2 to 2·6 Å in the gas phase and in acetonitrile), giving rise to a coordination number of 8. When Cl^- counterions are added in the simulation, initially at about 3·5 Å from Eu^{3+}, one of them becomes coordinated directly to Eu^{3+} *in vacuo* as in acetonitrile (at 2·4 Å), while the two others are remote (at 5·2 and 7·3 Å *in vacuo*, 7·4 and 8·1 Å in acetonitrile). As a result of the hindrance due to the bound Cl^-, one of the four bipyridine arms loses completely the Eu^{3+} coordination (N–Eu^{3+}>5 Å), while two arms remain bidentate (Eu^{3+}–N at about 2·2 Å), and another one loosely bidentate (N–Eu^{3+} at 2·2 and 3·2 Å). These LIGI–$EuCl_3$ complexes are very similar in acetonitrile and *in vacuo*.

The energy component analysis fully supports these structural data. The average values obtained in acetonitrile are reported in Table 3. They show that the large Eu^{3+}–LIGI attraction energy stems mostly from the four bipyridine arms (about 96% without and with Cl^- counterions). In the absence of anions, each of the four bipyridines interacts to a similar, but not identical extent with Eu^{3+} (from -177 to -205 kcal mol^{-}), indicating some deviation from the fourfold symmetry of the complex. However, in the presence of Cl^- anions, the interactions of Eu^{3+} with the bipyridines of LIGI become much less attractive (by about 120 kcal mol^{-1}) because the bipyridine remote from Eu^{3+} interacts weakly (about -30 kcal mol^{-1} versus -150 to 200 kcal mol^{-1} for the other bipyridines).

There are important interactions between the acetonitrile solvent and the complex (-258 and -194 kcal mol^{-1}, with Eu^{3+} and $EuCl_3$ complexes respectively). Those attrac-

Table 1. Average interaction energies (kcal mol^{-}) for the free ligands in different environments[a]

	Gas phase				Acetonitrile				Water		
Energy	LIGI	LIGII	LIGIII[b]	LIGIV	LIGI	LIGII	LIGIII[b]	LIGIV	LIGI	LIGII	LIGIII
$E(1/2+3+4)$	−17·6	−5·0	0·0	−12·6	−14·5	−4·7	−0·9	−13·5	−5·6	−2·7	−1·2
$E(2/1+3+4)$	−14·6	−8·6	0·0	−18·4	−14·6	−12·8	−16·6	−18·0	7·5	1·2	0·1
$E(3/1+2+4)$	−13·7	−12·5	−18·7	−12·0	−13·0	−5·2	−14·8	−12·8	10·4	2·8	0·0
$E(4/1+2+3)$	−24·1	−5·0	−18·7	−11·7	−12·0	−12·3	−6·7	−12·2	2·4	−3·3	−1·5
(bpy)4–solv[c]	–	–	–	–	−92·0	−115·5	−129·2		−276·8	−164·2	−222·4

[a] $E(i/j+k+l)$ is the interaction energy of the branch i with the branches j, k, l. The averages are taken over 100 ps.

[b] For this ligand there are only two bipyridines in close contact. The other two are completely separated.

[c] Interaction energy (kcal mol^{-1}) of the four bipyridine branches with the solvent.

Statistical fluctuations are between 1·0 and 4·0 kcal mol^{-1} for the $E(i/j+k+l)$ contributions and about 3·0 kcal mol^{-1} for the (byp)4–solv contributions.

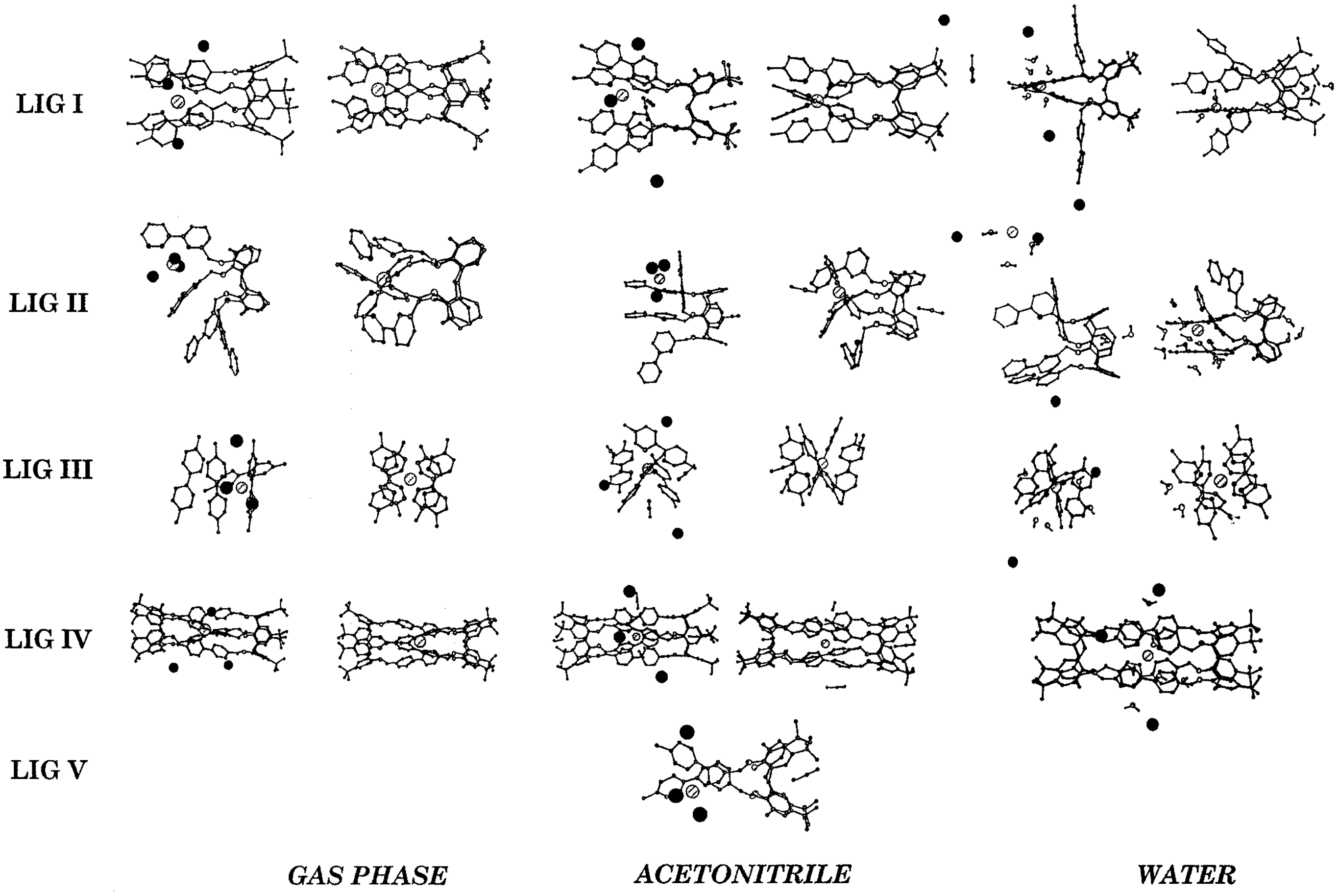

Figure 3. Complexes with $EuCl_3$ and Eu^{3+} in different environments. Snapshots after 220 ps of simulation in the gas phase and in acetonitrile and after 120 ps of simulation in water. The Cl^- ions are drawn as dark circles

Table 2. Coordination numbers of the complexed Eu^{3+} cation at the end of simulations[a]

	Gas phase					Acetonitrile							Water						
	Eu^{3+}		$EuCl_3$			Eu^{3+}			$EuCl_3$				Eu^{3+}			$EuCl_3$			
	CN	n_N	CN	n_N	n_{Cl}	CN	n_N	n_S	CN	n_N	n_{Cl}	n_S	CN	n_N	n_S	N_T	n_N	n_{Cl}	n_S
LIGI	8	8	7	6	1	8	8	0	7	6	1	0	8	6	2	8	4	0	4
LIGII	6	6	3	0	3	6	6	0	6	4	2	0	4	4	0	7–8	0	1	6–7
LIGIII	8	8	7	6	1	8	8	0	8	8	0	0	8	8	0	8	8	0	0
LIGIV	8	8	8	8	0	8	8	0	8	8	0	0	8	8	0	8	8	0	0
LIGV	Not studied					Not studied			6	4	2	0	Not studied						

[a] $CN = n_N + n_{Cl^-} + n_s$, where n_N, n_{Cl^-} and n_s are the contributions of Npyridine, Cl^- anions and solvent coordinated atoms, respectively.

tions come from charge–dipole interaction with one MeCN molecule which sits inside the cone of LIGI, pointing its N atom towards the cation (Figure 3) and from medium- and long-range Eu^{3+}–acetonitrile interactions. As the counterions added in the simulation remove some solvent molecules and prevent an optimal orientation of their dipoles with respect to Eu^{3+}, the $EuCl_3$ complex interacts less with acetonitrile than does the Eu^{3+} complex. On the other hand, the ligand LIGI itself, more open and accessible to the solvent in the $EuCl_3$ complex than in the Eu^{3+} complex, is better solvated (LIGI–solvent interactions are −102 and −55 kcal mol^{-1}, respectively). This analysis thus makes clear that solvation contributes significantly to the energy balance within these complexes.

In water, the LIGI–Eu^{3+} complex has, during most of the simulated time, the four bipyridine arms coordinated to the cation. However, at about 80 ps, one arm opens (Figure 4), leaving the three others bound to the cation, with N–Eu^{3+} distances of 2·3–2·4 Å. Two water molecules complete the first coordination sphere of Eu^{3+}.

The most dramatic solvation effect is found in water for the LIGI–$EuCl_3$ complex, which becomes only ‘two-branched’, with four water molecules in the first coordination shell of Eu^{3+}, giving rise to a total coordination number of eight. No anion is found at less than 8 Å from Eu^{3+}. The other two bipyridines have moved away, at 6–10 Å from Eu^{3+}, from an axial to equatorial position with respect to the calixarene C_4 axis (Figure 3). In Figure 5 are reported time evolutions of the N_{12}–Eu^{3+} distance relative to one of the two opening bipyridine arms, together with the interaction energies $E_{host–Eu^{3+}}$, $E_{host–water}$, and $E_{Eu^{3+}–water}$. When two bipyridine arms of the ligand open (the N_{12}–Eu^{3+} distance increases from 3·0 to 8·0 Å), the decrease in Eu^{3+}–host interaction (about 150 kcal mol^{-}) is more than

Table 3. Energy component analysis of complexes in solution[a].

	Eu^{3+}				$EuCl_3$					
	LIGI	LIGII	LIGIII	LIGIV[e]	LIGI	LIGII	LIGIII[ax][f]	LIGIII[eq][f]	LIGIV[e]	LIGV
In acetonitrile:										
Eu^{3+}–Calix[b]	−24	−27	–	−25; −27	−24	−20	–	–	−27; −27	−24
Eu^{3+}–(bpy)4[c]	−758	−489	−800	−776	−596	−314	−795	−750	−725	−159
Eu^{3+}–$3Cl^-$[d]	–	–	–	–	−646	−885	−446	−426	−388	−927
Solute–solvent	−258	−346	−266	−143	−194	−196	−168	−199	−269	−149
In water:										
Eu^{3+}–Calix[b]	−25	−26	–		−23	−4	–	–	−25; −25	
Eu^{3+}–(bpy)4[c]	−737	−422	−799		−425	−21	−799	−799	−782	
Eu^{3+}–$3Cl^-$	–	–	–		−314	−580	−138	−122	−308	
Solute–solvent	−361	−534	−315		−1016	−1192	−605	−670	−613	

[a] Averages over 200 ps for acetonitrile simulations and over 100 ps for water simulations.
[b] Interaction energy between Eu^{3+} and the ligand calixarene fragment.
[c] Interaction energy between Eu^{3+} and the four bipyridines.
[d] Interaction energy between Eu^{3+} and the three anions.
[e] For LIGIV the two numbers are relative to the two calixarene fragments. Statistical fluctuations range from 2 to 5 kcal mol^{-1} for Eu^{3+}–Calix and 10–30 kcal mol^{-1} for all the other contributions.
[f] LIGIII^{ax} and LIGIII^{eq} represent the two starting structures as described in the Experimental section.

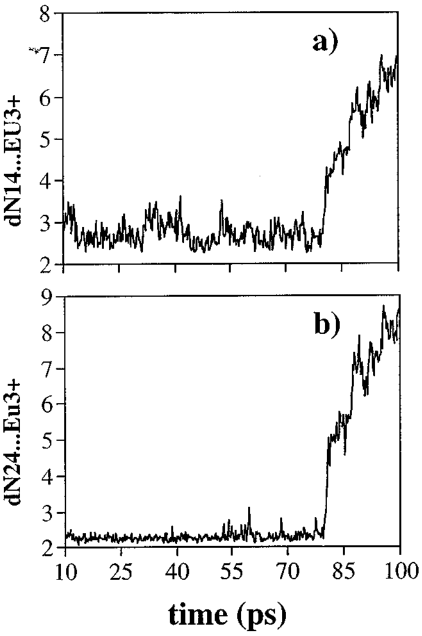

Figure 4. Time evolution plots for the LIGI–Eu^{3+} complex in water. (a) N_{41}–Eu^{3+} and (b) N_{42}–Eu^{3+} distances relative to the opening arm

compensated for by the increased hydration energy of Eu^{3+} and of the host (about 200 and 80 kcal mol^{-1}, respectively).

LIGII 'complexes' with Eu^{3+} and $EuCl_3$

The gas-phase calculations on LIGII–Eu^{3+} make it clear that, unlike LIGI, LIGII is a poor ion binder (see Figure 3 and Table 2).

In the gas phase, only three bipyridines coordinate Eu^{3+} with Eu^{3+}–N distances of about 2·3 Å. Two of them are bound via one N atom only, the second N atom being at about 3·6 Å from the cation. In the presence of Cl^- counterions, none of the bipyridines binds Eu^{3+}, because the three anions make intimate contacts with Eu^{3+} (at about 2·4 Å). In solution as expected, the complexes are still weakened. In acetonitrile the Eu^{3+} complex (no Cl^-) has three bipyridines bound to Eu^{3+} (distances of about 2.3 Å), and the fourth one at about 5·6–5·8 Å. In the presence of counterions, two bipyridine arms still bind Eu^{3+}, while the other two are repulsed by the two Cl^- anions bound to Eu^{3+}.

In water the structure of the LIGII–Eu^{3+} complex, at the end of the simulated time, is only 'two-branched,' with four N atoms at about 2·3 Å and the four others at 5·1–5·9 Å from Eu^{3+}. The LIGII–$EuCl_3$ complex dissociates completely. All N–Eu^{3+} distances range between 7·8 and 13·4 Å. One Cl^- ion only is in proximity of the Eu^{3+} cation, at a distance of 3·0 Å. Thus, although the precise structure and solvation of the LIGII 'complexes' depends on its environment, it is clear that LIGII cannot complex a cation properly.

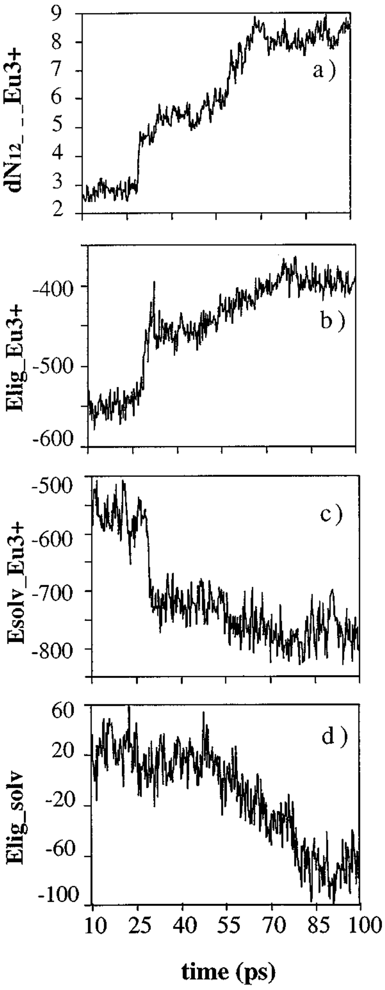

Figure 5. Time evolution plots for the LIGI–$EuCl_3$ complex in water. (a) N_{12}–Eu^{3+} distance relative to one of the opening bipyridine arms. (b–d) Interaction energies, $E_{\text{host–Eu}^{3+}}$, $E_{\text{host–solv}}$ and $E_{\text{Eu}^{3+}\text{–solv}}$, of the ligand with Eu^{3+}, of the ligand with the solvent and of Eu^{3+} with the solvent respectively.

Role of the calix[4]arene platform in organizing four bipyridine units inthe Eu^{3+} and $EuCl_3$ complexes. Comparison of LIGI, LIGIII and LIGIV

As expected, anchoring of the four bipyridine units at the lower rim of one or two calix[4]arene moieties modifies strongly the structure and cation surrounding the Eu^{3+} and $EuCl_3$ complexes. In this section, we compare the com-

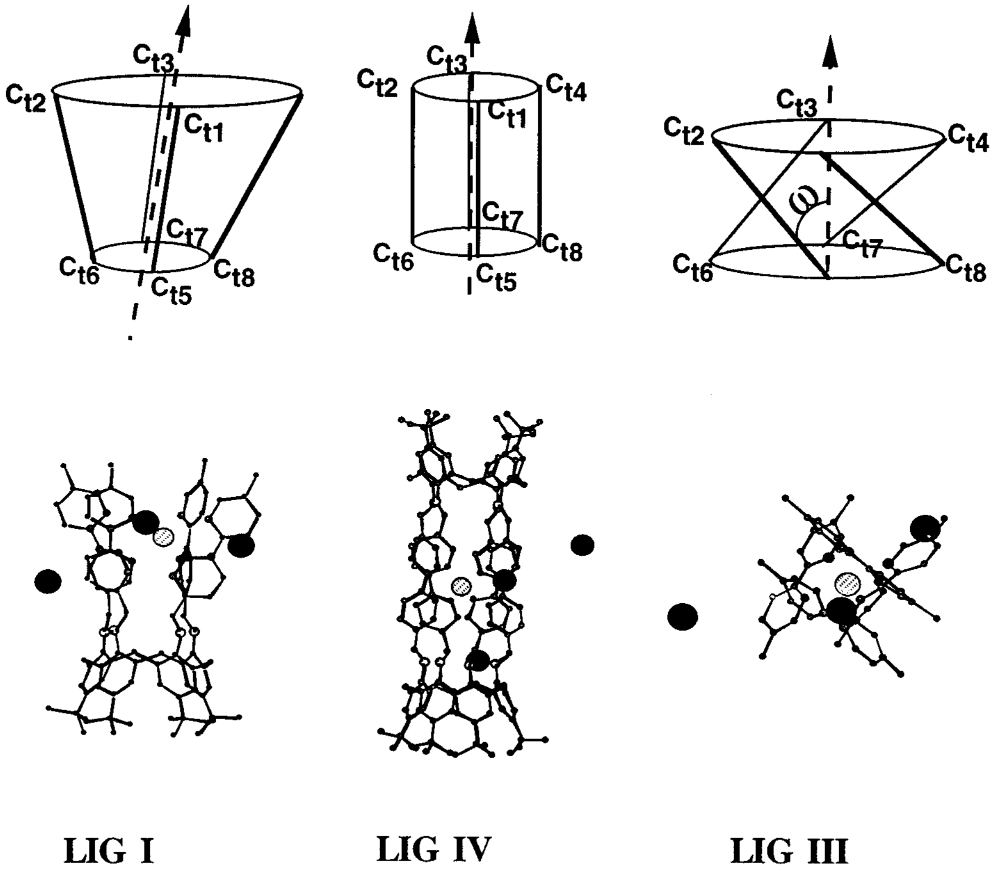

Figure 6. Schematic representation of the shape of the four-bipyridine cage: distorted truncated cone for LIGI, regular cylinder for LIGIV and twisted cylinder for LIGIII

plexes of LIGI with those of LIGIII and LIGIV, where the four bipyridines are unconnected and rigidfied by two anchoring platforms, respectively.

In these complexes, Eu^{3+} makes short contacts with seven or eight $N_{pyridine}$ atoms (2·0 to 2·7 Å), and is shielded from the acetonitrile or water solvent. The only exception, reported above, is the $EuCl_3$ complex of LIGI, which opens somewhat in water. There are, however, interesting differences in the shaping of the $(bipyridine)_4$ fragment, depending on its conformational freedom and anchoring to the calixarene moiety. For a given ligand this fragment has roughly the same shape *in vacuo* and in solution. Schematically, it is a distorted truncated cone for LIGI, a regular cylinder for LIGIV and a twisted cylinder for LIGIII (Figure 6).

In order to quantify some of the 'cone/cylinder parameters' of the $EuCl_3$ complexes, we calculated the opposite C_t–C_t distances (Figure 6 and Table S–IV, Supplementary material), and the tilt angle ω between the cone axis and each bipyridine 'axis.' The cone axis is defined by the line joining the 'upper' and 'lower' C_t carbons (Figure 6); the axis of a given bipyridine joins its $C_{t(upper)}$ and $C_{t(lower)}$ atoms.

The LIGI–$EuCl_3$ complex in acetonitrile has three opposite C_t–C_t distances between 5.0 and 6.0 Å, and one more elongated (15·0 Å), giving rise to the distorted truncated cone, with three ω angles between 20° and 60° and one ω angle close to 80°. The same complex behaves differently in water, as already discussed, and the two opening arms have ω angles of about 80° (Table S-V, Supplementary material).

The LIGIV complexes are more symmetrical, with the four C_t–C_t opposite distances of comparable values (about 6.0 Å in the gas phase, acetonitrile and water). The shape of the bipyridine cage is a regular cylinder (ω angles of about 16°). In acetonitrile one solvent molecule resides in each of the calixaene cavities, pointing the methyl group and the N atom toward the cation (see Figure 3). In the Eu^{3+} and $EuCl_3$ complexes, the cation is coordinated at about 2·5 Å to the eight $N_{pyridine}$ atoms in the gas phase and in solution. The three Cl^- counterions are somewhat more remote from Eu^{3+} in acetonitrile than in the gas phase (8·1, 8·2 and 5·5 Å). The cation is shielded fromthe solvent in acetonitrile and in water.

The unlinked bipyridines of LIGIII have more freedom to wrap around the cation. Opposite C_t–C_t distances are about 6·0 and 9·0 Å in solution. The general shape of the bipyridines is a twisted cylinder (Figure 6) with ω angles of about 30°. After 220 ps *in vacuo* LIGIII–$EuCL_3$ is ‘three-branched’ because one Cl^- anion binds to Eu^{3+}. In all the other simulations however, without or with counterions, the four bipyridines wrap completely around Eu^{3+}, with eight N–Eu^{3+} distances of 2·30–2·38 Å and no direct coordination of Cl^- to Eu^{3+}. In acetonitrile, the two starting structures of the $EuCl_3$ complex (which differ by the ‘axial’/‘equatorial’ position of one Cl^-) converge to the same one, where the three anions are remote from Eu^{3+} (at 6·6–8·3 Å) which is bound to the eight N atoms (at 2·25–2·41 Å). LIGIII therefore provides the optimum surrounding to Eu^{3+} in the gas phase and in solution. From the calculations, however, it is not clear whether the stability of this simulated complex is of a kinetic or thermodynamic nature.

Given the similar Eu^{3+} environment of the four ligating bipyridines in LIGI, LIGIII and LIGIV, it is interesting to compare the interaction energy between Eu^{3+} and the $(\text{bipyridine})_4$ fragment (Table 3) in solution. It is very attractive and similar for the three ligands in acetonitrile and water, with or without counterions (500–800 kcal mol^{-1}). It is noteworthy that the attraction is about 25 kcal mol^{-1} larger in LIGIII than in LIGIV, owing to the relaxation of LIGIII and the rigidity of LIGIV, which does not allow for optimal interactions with Eu^{3+}. In the LIGI–$EuCl_3$ complex, this interaction energy is weaker in all the explored environments (596 and 425 kcal mol^{-1} in acetonitrile and water, respectively), because it is ‘three-branched’ *in vacuo* and in acetonitrile, and still more open in water, while the LIGIII and LIGIV complexes are ‘four-branched.’

Number of effective bipyridine arms: are two arms sufficient to complex Eu^{3+}?

In order to clarify the optimum number of bipyridines to be attached to the calixarene platform to wrap efficiently around the cation, we studied in acetonitrile the $EuCl_3$ complex of LIGV, which derives from LIGI by substitution of two opposed bipyridines by two methoxy groups. Thus, the cation can be bound to, at most, two bipyridine arms. As can be seen from Figure 3, after 200 ps the cation is still coordinated to the two bipyridines (at about 2·2 Å) and to two Cl^- ions (at about 2·4 Å). As the cation is shielded from solvent, its coordination number is six. Thus two bipyridines seem to be enough to complex Eu^{3+}, provided that counterions contribute to cation shielding from the solvent. In the absence of counterions, solvent molecules would bind to Eu^{3+}, assist its decomplexation and quench its luminescence, if any.

Complexes of calix[4]arenes substituted by two 6,6′-bipyridines and two amide arms have recently found to be weakly luminescent.[10] In this ligand, the bipyridines are connected to the calixarene framework as in LIGII, which has been shown above to be a poor cation binder. We suggest that substitution by 5,5′-bipyridines as in LIGI would enhance the stability and luminescence complexes of these mixed complexed.

CONCLUSIONS

We have presented a theoretical study of Eu^{3+} complexes of a series of bipyridine ligands LIGI–LIGV of unknown structure. These complexes differ in the type and degree of connectivity to a calix[4]arene platform. They were simulated in different environments in the gas phase and in acetonitrile and water solutions, without and with counterions. Our results demonstrate the versatility of the lanthanide ion surrounding, as a result of the competitive non-covalent interactions between the cation, the ligand, the counterions and the solvent. In particular, the difference in luminescence properties of Eu^{3+} complexes of LIGI compared with LIGII relates to their difference in stabilities and ion shielding from the solvent.

Our simulations used a pairwise 1–6–12 additive potential to represent these non-covalent interactions. The electrostatic interactions are thus represented by a coulombic term, without explicit account of the polarization and many-body energy components. This is a rough approximation which hopefully provides the gross structural features of the system, but will require force field developments.

For a given ligand, we find that the number of bipyridine arms coordinated to $Eu^{3+}$is similar in the gas phase and in acetonitrile, but may be less in water, owing to the solvation of Eu^{3+} and of the ligand. The number of bipyridines bound to Eu^{3+} may depend markedly on the counterions. For example, ‘four-branched’ (LIGIII, LIGIV), ‘three-branched’ (LIGI) and ‘two-branched’ (LIGV) complexes have zero, one and two Cl^- counterions, respectively, bound to Eu^{3+}. The loss of Eu^{3+}–bipyridine attractions is thus compensated for by the cation–anion attractions in solution. It is clear that replacement of Cl^- by a smaller anion such as F^- would favour the anion coordination to the Eu^{3+}, whereas more bulky anions would be more remote from Eu^{3+}, leading to enhanced interactions and possible ‘antenna effects’ between Eu^{3+} and the ligand.

The calculated Eu^{3+} coordination number is eight and is largest for LIGI, LIGIII and LIGIV in the three environments explored (Table 2). Nevertheless, the spatial disposition of the bipyridines is very different in the three cases. Complexes of LIGI, which are luminescent, are almost always ‘three-branched’ (Figure 3), suggesting that three bipyridine arms are probably enough to wrap the cation efficiently and to allow for the ‘antenna effect.’ This is supported by experiment: the calix[4]arene derivative bearing only three 5,5′-bipyridine substituents presents a luminescence quantum yield very similar to LIGI (Φ 14 vs 16%).[17] This contrasts with LIGII–Eu^{3+}, which displays a very weak luminescence, and is calculated here not to be stable. In fact, in all the 'complexes' of LIGII, the Eu^{3+} cation is more exposed to the solvent and to the counterions, and loosely bound to the ligand.

The comparison of complexes with LIGIII and LIGIV, where the cation is surrounded by four bipyridines, reveals subtle conformational problems. In LIGIII, the four bipyridines adopt an 'optimum' arrangement around Eu^{3+}, and shield it completely from the solvent and counterions in solution. On the other hand, the bipyridines of LIGIV, maintained by the two calixarene platforms, delineate a rigid cage, which prevents solvent or anion coordination to the complexed cation. Significant 'antenna effect' and luminescence are thus anticipated with LIGIII and LIGIV ligands. No related data are available, but presumably for different reasons. In the absence of an anchoring platform, the four bipyridines of LIGIII are dissociated and the energy cost in assembling them may prevent the formation of a stable complex. Our simulated LIGIII complex would therefore be thermodynamically unstable. In the case of LIGIV, the complex should be thermodynamically stable, but probably involves a too high kinetic energy barrier. The rigidity of this host prevents solvent and counterion assistance for the lanthanide diffusion inside the bipyridine cavity.[7] Thus, trapping of the cation during the synthesis of the ligand, before the cavity is locked, is expected to lead to a kinetically and thermodynamically stable complex, which should be luminescent.

In most of the simulated complexes, the presence of explicit counterions has been found to modify strongly the coordination pattern of Eu^{3+} and the overall structure of complexes. It is therefore anticipated thatthe nature, size, binding and solvation features of the counterion will modulate markedly the luminescence properties of the complexed cation.

Another important result is the different behaviour of complexes in water compared with acetonitrile solution. These simulations therefore strongly suggest that when the acetonitrile solution is not completely dry, traces of water may compete with the ligands and counterions to bind Eu^{3+} and quench its luminescence.

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Note Added in Proof

An independent theoretical study, very closely related to this one, has been performed on $Eu(NO_3)_3$ complexes of calix[4]arene ligands in acetonitrile, reaching similar conclusions to those presented here.[49] WG would like to thank the author for this information.

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