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Complexation of Calix[4]arene Derivatives and Trivalent Cations in Dipolar Aprotic Media

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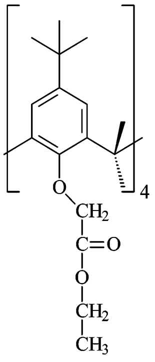
The complexation of *p-tert*-butylcalix[4]arene tetraethanoate, **1a**, *p-tert*-butylcalix[4]arene tetramethyl ketone, **1b**, and *p-tert*-butylcalix[4]arene tetraacetamide, **1c**, and trivalent cations was investigated in acetonitrile and *N*,*N*-dimethylformamide at 298.15 K using several techniques. ^{1}H NMR measurements in CD_3CN at 298 K were carried out for the systems involving **1a**, **1b**, and **1c** as ligands and Sc^{3+}, Y^{3+}, Eu^{3+}, and Yb^{3+} as cations. For the latter ligand, ^{1}H NMR titration with La^{3+} was also carried out to assess the sites of interaction of these ligands and the appropriate cation in this solvent. Conductance measurements were performed in acetonitrile and *N*,*N*-dimethylformamide with the aim of determining the composition of the metal ion complexes. Stability constants and derived standard Gibbs energies, enthalpies, and entropies reveal that, as far as **1b** is concerned, this ligand is not able to distinguish among the trivalent cations as a result of a remarkable enthalpy−entropy compensation effect. This is not the case for **1c** and these cations in acetonitrile and to a lesser extent in *N*,*N*-dimethylformamide. The selective behavior of this ligand for these metal cations is reflected in the stability constants, which are higher in acetonitrile than in *N*,*N*-dimethylformamide. A plot of log K_s values against the cation radius shows a "selectivity" peak. In acetonitrile, the complex stability is greater than that previously observed for an analogous derivative and these cations in this solvent. The medium effect on the complexation process is discussed.

Introduction

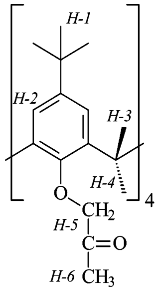
Calixarenes have gained an important place in host−guest chemistry because of their ability to form complexes with ions and neutral molecules.[1−4] In particular, functionalization of the lower rim (phenolic OH groups) of calix[4]arene with suitable binding groups has produced a series of new, powerful, and selective cation receptors and carriers.[2−4] The coordination properties of such ligands are tuned by appropriate choice of substituents differing in hydrophilicity−hydrophobicity and the number and the type of donor atoms present among other factors. The trivalent cations, namely, lanthanides (Ln^{3+}), can interact with such synthetic ligands containing suitable donor atoms to yield complexes of the guest−host type. The Ln^{3+} affinity to donor atoms is in the decreasing order O > N> S. They have coordinations numbers[5] ranging from 8 to 12. Thus, calixarene derivatives containing oxygen and nitrogen donor atoms would be expected to interact strongly with such metal cations.

Although the preparation and characterization of solid complexes of lanthanide(III) metal cations with macrocyclic compounds have been reported,[6] only a few thermodynamic studies for these systems have been carried out. The Ln^{3+} complexation in nonaqueous media is important from the point of view of separation and purification of lanthanides.[7] However, most data reported on the interactions of calixarene derivatives and Ln^{3+} are limited to the determination of the stability constant, while enthalpy and entropy data for these systems have not been determined. A recent study for the complexation of calixarene derivatives and Ln^{3+} in nonaqueous media has been reported by Danil de Namor and Jafou.[7−8]

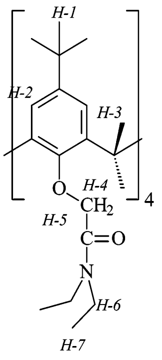
The present study is related to the interaction between three calix[4]arene derivatives, namely, *p-tert*-butylcalix[4]arene tetraethanoate, **1a**, *p-tert*-butylcalix[4]arene tetramethyl ketone, **1b**, and *p-tert*-butylcalix[4]arene tetraacetamide, **1c**, and trivalent cations in two dipolar aprotic solvents, namely, acetonitrile, MeCN (protophobic), and *N*,*N*-dimethylformamide, DMF (protophilic).



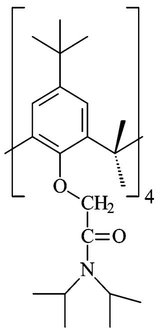
1a



1b



1c



1d

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The aims of this paper are (1) to use ^{1}H NMR spectroscopy to establish the absence/presence of complexation and the sites of interaction of calix[4]arene derivatives (**1a**, **1b**, and **1c**) in their complexation with trivalent cations in MeCN and DMF at 298.15 K, (2) to determine the composition of the trivalent cation complexes in these solvents via conductance measurements, and (3) to measure the thermodynamic parameters of complexation of these ligands and trivalent cations in these solvents at 298.15 K using various methods.

Experimental Section

Chemicals. Scandium (99%), yttrium (98%), lanthanum (99.9%), praseodymium (99%), neodymium (99%), europium (99%), gadolinium (99%), terbium (99%), holmium (99%), erbium (99%), ytterbium (99.9%) trifluoromethanesulfonate (triflates) salts, silver perchlorate (99.9%), and tetra-*n*-butylammonium perchlorate, TBAP (≥99%), were all purchased from Aldrich Chemical Co. Further drying of the lanthanide triflate salts was chemically performed using triethylorthoformate.[9] All the salts were stored over P_4O_{10} under vacuum for several days before use.

The macrocycles **1a**, **1b**, and **1c** were synthesized at the Thermochemistry Laboratory according to the procedure reported in the literature.[10,11] They were dried in a piston drier at 80−90 °C for several days before use.

MeCN,[12] HPLC grade from Fisher, was refluxed in a nitrogen atmosphere and distilled from calcium hydride. Only the middle fraction of the solvent was collected. DMF,[12] HPLC grade from Fisher, was dried over magnesium sulfate and subsequently distilled under reduced pressure. The middle fraction of the solvent was used.

Deuterated acetonitrile (CD_3CN) and tetramethylsilane (TMS) were purchased from Aldrich Chemical Co. CD_3CN was dried by adding magnesium sulfate and leaving it for several days before use.

^{1}H NMR Measurements. ^{1}H NMR measurements were performed for the trivalent cations Sc^{3+}, Y^{3+}, Eu^{3+}, and Yb^{3+} with **1a** and **1b**, and for Sc^{3+}, Y^{3+}, La^{3+}, Eu^{3+}, and Yb^{3+} with **1c** in CD_3CN at 298 K according to the reported procedure.[7] The solution concentration for the trivalent cation salts used was around 1.2×10^{-3} mol·dm^{-3}, while the concentration of the ligand solutions used was around 1.4×10^{-4} mol·dm^{-3}.

Conductance Measurements. The conductometric titration experiments were performed according to the reported procedure[7] for these ligands with the trivalent cations La^{3+}, Pr^{3+}, Nd^{3+}, Eu^{3+}, Gd^{3+}, Tb^{3+}, Er^{3+}, Ho^{3+}, Yb^{3+}, Sc^{3+}, and Y^{3+} as triflates. These trivalent cations (Ln^{3+}) were chosen to represent the whole series of the trivalent cations. It should be noted that Sc^{3+} and Y^{3+} were included in this series because the former cation has intermediate behavior between those of Al^{3+} and lanthanide cations while the atomic radius of Y^{3+} is close to that of Tb^{3+}. An important precaution to be taken when working with Ln^{3+} salts is to ensure that, at the range of Ln^{3+} salt concentrations used, ionic species are predominantly in solution.[7−8,13] Therefore, the concentration of the trivalent cation salts in MeCN and DMF ranged from 9.7×10^{-6} to 2.7×10^{-5} mol·dm^{-3}, while the ligand concentration was around 3.8×10^{-4} mol·dm^{-3}.

Conductance readings after each addition of the ligand solution into the reaction vessel containing the metal cation salt solution in the appropriate solvent were recorded after allowing enough time (20 min) for the solution to attain thermal equilibrium (conductance readings were constant).

Determination of the Stability Constant by UV Spectrophotometric Titration. The UV titration experiments were carried out with a CECIL 8000 series spectrophotometer in MeCN at 298 K with the aim of determining the stability constant[14] (log K_s) for **1b**−Ln^{3+} in this solvent. These titration experiments were accomplished through a stepwise addition of the Ln^{3+} solutions (0.01 mL, $\sim 7.8 \times 10^{-4}$ mol·dm^{-3}) to a solution of **1b** (1.5 mL, $\sim 5.0 \times 10^{-5}$ mol·dm^{-3}) in MeCN in the UV quartz cell. This was followed by a 15 min interval (in which the reaction cell was left under continuous stirring to ensure mixing). Then the UV data were collected and processed using a Hyperquad program[15] to calculate the stability constant (log K_s) of the appropriate cation(III) complex.

Microcalorimetric Titrations. The four-channel heat conduction microcalorimeter (Thermometric, 2277 thermal activity monitor) designed by Suurkuusk and Wasdö[16,17] was used. To check the reliability of the equipment, the chemical calibration reaction described by Wadsö[17] for the complexation of 18-crown-6 and barium (chloride as the counter ion) in aqueous medium at 298.15 K was carried out. The reaction vessel was charged with a solution of 18-crown-6 in water (2.8 cm^3), and about 14 injections were made with an aqueous solution of $BaCl_2$ contained in a Hamilton gastight syringe. Separate dilution experiments were performed to correct for dilution. The values obtained (log $K_s = 3.77 \pm 0.01$, $\Delta_c H° = -31.42 \pm 0.02$ kJ·mol^{-1}) were in good agreement with the ones published.[18]

The procedure for the microcalorimetric titration experiments was carried out in MeCN at 298.15 K as described elsewhere.[7] The concentrations of the ligand solutions used ranged from 4.9×10^{-5} to 2.4×10^{-4} mol·dm^{-3}, while the concentration of the Ln^{3+} salts solutions ranged from 1.8×10^{-4} to 7.3×10^{-4} mol·dm^{-3}. A computer program (Digitam 4.1 for Windows from Thermometric AB and Scitech Software AB, Sweden) was employed to calculate log K_s and $\Delta_c H$ values.

Determination of the Stability Constant by Competitive Potentiometric Titrations at 298.15 K. The competitive potentiometric titration method was used following the procedure established by Cox and Schneider, based on a competitive reaction between the trivalent cation and an auxiliary cation (Ag^+) as described elsewhere.[19−22] From potential readings the stability constant values of the Ln^{3+}−**1c** complexes in MeCN and DMF at 298.15 K were calculated. The concentrations of the specified ligand solutions were around 1.7×10^{-4} mol·dm^{-3} in both solvents, while those for the appropriate Ln^{3+} salts solutions in the appropriate solvent were around 4.5×10^{-4} mol·dm^{-3}. The Hyperquad program[15] was used to calculate the stability constant of the metal ion complex.

Results and Discussion

^{1}H NMR Titration of Calix[4]arene Derivatives and Trivalent Cations (Ln^{3+}) in CD_3CN at 298 K. *^{1}H NMR Titration Studies of* **1a** *and Ln^{3+} Cations.* ^{1}H NMR measurements were performed for the trivalent cations Sc^{3+}, Y^{3+}, Eu^{3+}, and Yb^{3+} with **1a** in CD_3CN at 298 K. However, the addition of these trivalent cations to **1a** solution did not show any significant changes in the chemical shifts of this ligand in this solvent. Thus, the data for these studies were not conclusive.

^{1}H NMR Titration Studies of **1b** *and Ln^{3+} Cations.* The proton chemical shift changes of Sc^{3+}−**1b**, Y^{3+}−**1b**, Eu^{3+}−**1b**, and Yb^{3+}−**1b** complexes relative to the free ligand are tabulated in Table 1. Inspection of the ^{1}H NMR titration appears to indicate that interaction takes place between **1b** and Sc^{3+}, Y^{3+} Eu^{3+}, and Yb^{3+} in CD_3CN. The ^{1}H NMR spectra for these cations showed a mixture of two signals (the free and the complexed

TABLE 1: Chemical Shift Changes ($\Delta\delta$, ppm)[a] in the ^{1}H NMR Spectra of 1b with Trivalent Cations in CD_3CN at 298 K

proton	$\Delta\delta$ (**1b**$-Sc^{3+}$)	$\Delta\delta$ (**1b**$-Y^{3+}$)	$\Delta\delta$ (**1b**$-Eu^{3+}$)	$\Delta\delta$ (**1b**$-Yb^{3+}$)
H-1	0.01	−0.02	-0.05	0.01
H-2	0.35	0.46	0.47	0.32
H-3 (equatorial)	0.14	0.15	0.14	0.13
H-4 (axial)	−0.14	unlabeled	-0.17	−0.17
H-5	0.20	0.81	0.21	0.16
H-6 (CH_3)	0.02	0.21	0.02	0.02

[a] Relative to the free ligand. Chemical shifts for **1b** (ppm): H-1, 1.16; H-2, 7.14; H-3 (equatorial), 3.27; H-4 (axial), 4.82; H-5, 4.77; H-6 (CH_3), 2.19.

ligand), which indicates that the complexation process in these systems is slow on the ^{1}H NMR time scale. However, at a 1:1 [Ln^{3+}]:[**1b**] ratio, the signals for the free ligand disappeared, which enabled identification of the signals for the complex formed.

Gutsche[2] noted that the difference between the chemical shifts ($\Delta\delta$, ppm) of the equatorial and axial protons of the methylene bridge provides information regarding the conformation of the calix[4]arene, where a difference of 0.90 ppm represents a system in a perfect "cone" conformation. The difference found for **1b** in CD_3CN was found to be 1.55 ppm for the free ligand, indicating that the aromatic rings become more parallel to each other while the macrocycle adopts a distorted cone conformation. However, upon complexation, the uptake of the metal cation by the hydrophilic cavity causes the pendent arms to become closer, leading to conformational changes. As a result, the difference between the equatorial and axial protons for the $Ln^{3+}-$**1b** complex was found to be 1.25 ppm, suggesting that the macrocycle adopts a more symmetrical cone conformation upon complexation. Significant chemical shift changes were also observed for the equatorial and H-5 protons (average of 0.14 and 0.19 ppm, respectively, Sc^{3+}, Eu^{3+}, and Yb^{3+}). As far as Y^{3+} is concerned, the most significant chemical shift changes were observed for H-5 and H-6 (0.81 and 0.21 ppm, respectively). However, the broadening of the equatorial chemical shift prevented its identification. These downfield shifts (deshielding effect) for these protons might be related to the encapsulation of the multicharged trivalent cation in the hydrophilic cavity. This would suggest that the lanthanide cation is centrally located within the hydrophilic cavity defined by the four ketone groups, interacting with the four ethereal and the four carbonyl oxygen atoms.

^{1}H NMR Titration Studies for **1c** *and Trivalent Cations.* The addition of the metal cations Sc^{3+}, Y^{3+}, La^{3+}, Eu^{3+}, and Yb^{3+} to a solution of **1c** in CD_3CN at 298 K produced broad and distorted proton signals which prevented analysis of the data in the case of La^{3+}, Y^{3+}, and Yb^{3+}. As far as the ^{1}H NMR data for Sc^{3+} and Eu^{3+} are concerned (see Table 2) the spectra became readable upon reaching a 1:1 [L]:Ln^{3+}] ratio. Hence, the chemical shift changes upon complexation of **1c** with Sc^{3+} and Eu^{3+} relative to the free **1c** were analyzed.

The difference observed between the axial and equatorial protons (2.05 ppm) in CD_3CN suggested that the ligand adopts a highly distorted cone conformation. This interpretation may find some support in the X-ray structure of this ligand reported in the literature,[23] although the latter is referred to the solid state. However, upon cation complexation this difference is reduced to 0.98 ppm, suggesting that **1c** adopt a symmetrical cone conformation similar to that of the parent calix[4]arene.[1] In addition, the large chemical shift changes observed for the aromatic protons might be related to the involvement of the ethereal oxygen donor atoms in the complexation process as well as to changes in the ligand conformation.

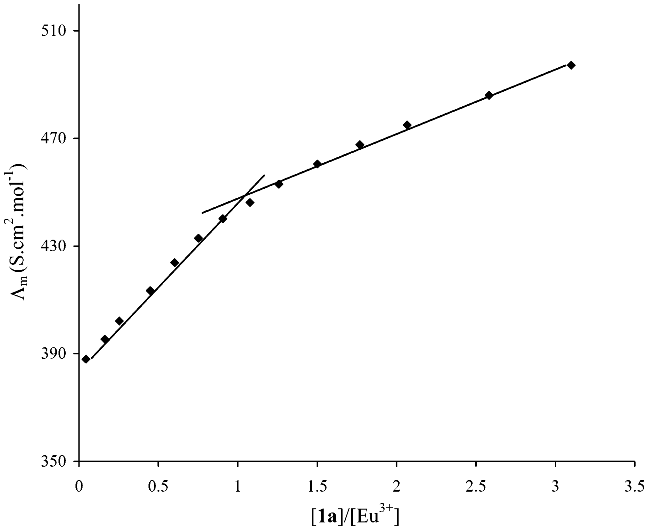

Figure 1. Conductometric curve for the titration of Eu^{3+} with **1a** in acetonitrile at 298.15 K.

TABLE 2: Chemical Shift Changes ($\Delta\delta$, ppm)[a] in the ^{1}H NMR Spectra of 1c with Trivalent Cations in CD_3CN at 298 K

proton	$\Delta\delta$ (**1c**$-La^{3+}$)	$\Delta\delta$ (**1c**$-Eu^{3+}$)	proton	$\Delta\delta$ (**1c**$-La^{3+}$)	$\Delta\delta$ (**1c**$-Eu^{3+}$)
H-1	0.02	0.04	H-5	−0.28	−0.21
H-2	0.88	1.40	H-6	overlapped	overlapped
H-3 (equatorial)	1.45	1.46	H-7 (CH_3)	0.77	0.80
H-4 (axial)	−0.22	0.56			

[a] Relative to the free ligand. Chemical shifts for **1c** (ppm): H-1, 1.14; H-2, 7.10; H-3 (equatorial), 3.16; H-4 (axial), 5.21; H-5, 4.98; H-6, 3.33; H-7 (CH_3), 1.21.

The significant chemical shift changes observed for the aromatic H-7 (CH_3) may suggest that the sites of interaction of **1c** with the cations are the oxygen donor atoms. Moreover, the structure of the $Eu^{3+}-$**1c** complex (triflate) reported by Sabbatini et al.[23] (solid state) shows that the four ethereal and the four carbonyl oxygen donor atoms are involved in the complexation of this cation with this ligand.

Conductometric Studies. Conductometric studies were conducted with ligands **1a**, **1b**, and **1c** and trivalent cations in two solvents, MeCN and DMF, at 298.15 K and are now discussed.

As far as **1a** is concerned, plots of molar conductance (Λ_m, S$\cdot$cm$^2\cdot$mol^{-1}) against the ligand:metal cation ratio ([**1a**]:[Ln^{3+}]) show that although 1:1 complexes are formed, they are relatively weak. Thus, Figure 1 shows the conductometric curve for the titration of Eu^{3+} with **1a** in MeCN at 298.15 K. An increase in conductance is observed. Moreover, the equilibrium position is shifted by the addition of the ligand to favor the formation of the complex cation (apparently less solvated than the free cation), and as a result the conductance increases slightly after 1:1 stoichiometry is achieved.

Likewise, conductometric titrations carried out for **1b** and trivalent cations in MeCN suggested the formation of 1:1 complexes in this solvent at 298.15 K. However, the results reveal two different conductance behaviors. Thus, for the light trivalent cations (La^{3+}, Sc^{3+}, and Y^{3+}) a decrease in conductance is observed upon the addition of the ligand to the metal cation until the 1:1 ratio is achieved. A representative example is given in Figure 2a for the conductometric titration of Y^{3+} with **1b** in

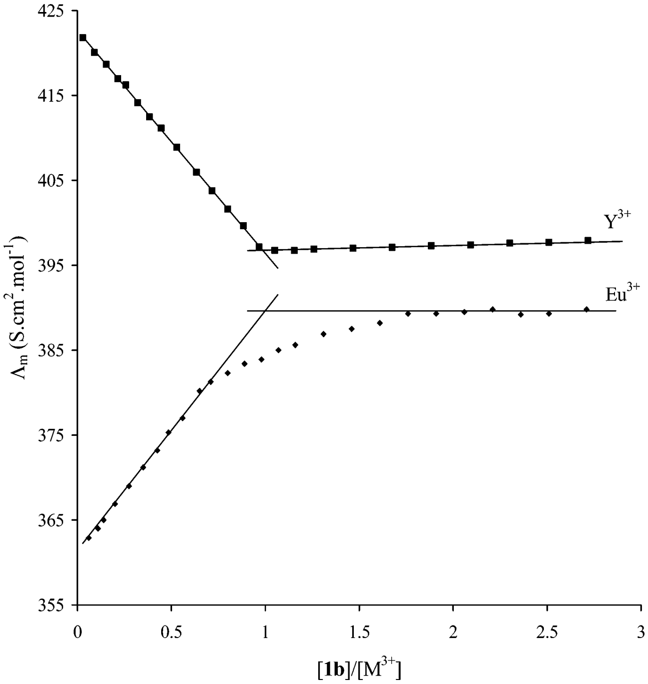

Figure 2. Conductometric curve for the titration of Y^{3+} (a) and Eu^{3+} (b) with **1b** in acetonitrile at 298.15 K.

acetonitrile at 298.15 K. This decrease in conductance is expected in moving from the free to the complex metal cation due to the increase in the size of the cation and the consequent decrease in mobility and hence conductivity. However, the opposite behavior is observed for the middle and late (heavy) trivalent cations (Nd^{3+}, Pr^{3+}, Eu^{3+}, Gd^{3+}, Tb^{3+}, Er^{3+}, Ho^{3+}, and Yb^{3+}) in this solvent. Thus, an increase in conductance is observed as complexation proceeds. This is demonstrated in the representative titration curve shown in Figure 2b for the Eu^{3+} cation and **1b** in MeCN at 298.15 K. These findings lead to the suggestion that the complex cation is less solvated than the free cation.[24,25] The observed difference in the conductance behavior of trivalent cations upon complexation has been previously observed in interactions involving light and heavy lanthanides.[26] This observation may be related to the lanthanide contraction and the change in the coordination number, which appear to occur at Nd^{3+} and Gd^{3+}.[27]

Conductance measurements of trivalent cations with **1b** in DMF did not show any sign of interaction between these cations and this ligand in this solvent.

However, conductance measurements performed with **1c** and trivalent cations in MeCN revealed the formation of relatively strong 1:1 complexes. This is illustrated in Figure 3, where the conductometric titration curve for Eu^{3+} and **1c** in MeCN at 298.15 K is shown. Quite a contrasting effect is shown for the same cation and **1c** in DMF (see Figure 4), which may illustrate the reverse behavior of solvation of the free and complex cation in these two solvents.

Having established the complex composition of these ligands and trivalent cations in these solvents, we proceeded with thermodynamic studies under conditions in which the free and complex cations are predominantly in their ionic forms in solution. This is discussed in the following section.

Thermodynamics of Complexation. As far as **1a** is concerned, microcalorimetric, ^{1}H NMR, and conductance studies revealed that very weak complexes are formed between this ligand and the trivalent cations in MeCN. Generally, for reactions with log K_s values lower than 2, the percentage of complex formed in the concentration range used is very small. Therefore, a large extrapolation is needed to calculate the complexation enthalpy of **1a** and trivalent cations in this solvent, and this may lead to erroneous data. Low stability of these complexes was also shown on the gradual decrease of potential vs time plots observed in the microcalorimetric titrations involving **1a** and trivalent cations, indicating a very weak interaction between **1a** and these cations in this solvent.[8]

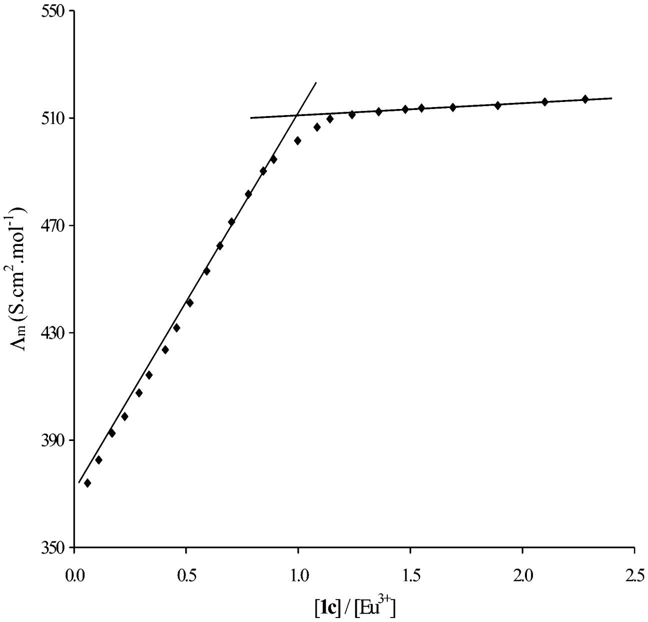

Figure 3. Conductometric curve for the titration of Eu^{3+} with **1c** in acetonitrile at 298.15 K.

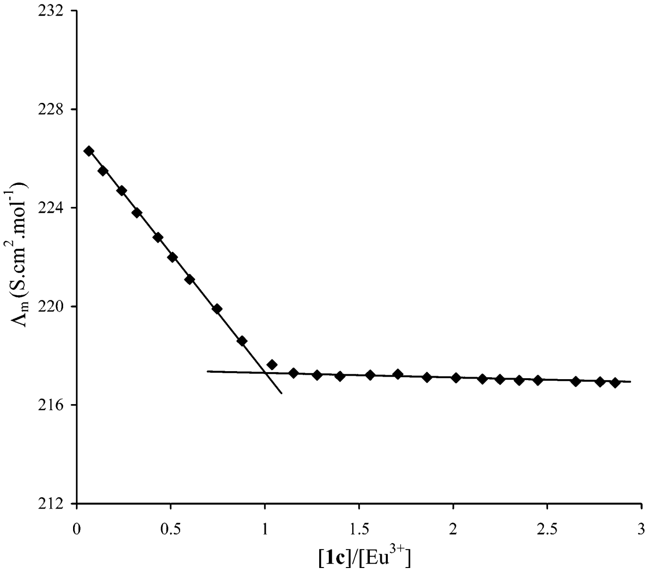

Figure 4. Conductometric curve for the titration of Eu^{3+} with **1c** in *N*,*N*-dimethylformamide at 298.15 K.

As far as **1b** and trivalent cations in MeCN are concerned, two methods were used to determine the stability constants. These were UV spectrophotometry and microcalorimetry. The latter has the advantage over the former in that it also allows the determination of the enthalpy associated to the complexation process. Thus, Table 3 reports the stability constants (expressed as log K_s values) derived from UV spectrophotometry and titration microcalorimetry. These data were used to derive standard Gibbs energies of complexation, $\Delta_c G°$. Enthalpies, $\Delta_c H°$, and entropies, $\Delta_c S°$, of **1b** and trivalent cations in MeCN

TABLE 3: Thermodynamic Parameter Data for the Process of Complexation for Ln^{3+}−1b in Acetonitrile at 298.15 K

cation^{3+}	ionic radius^{5}	log K_s		$\Delta_cG°$ (kJ·mol^{-1})	$\Delta_cH°$ (kJ·mol^{-1})	$\Delta_cS°$ (J·K^{-1}·mol^{-1})
Y(III)	0.93	4.47 ± 0.08[a] 4.52 ± 0.12[b]	4.50 ± 0.09[c]	−25.68 ± 0.13	−2.9 ± 0.1[b]	76
Sc(III)	0.72	4.43 ± 0.05[a] 4.49 ± 0.07[b]	4.46 ± 0.06[c]	**−25.46 ± 0.07**	**−5.0 ± 0.1[b]**	69
La(III)	1.06	4.45 ± 0.06[a] 4.54 ± 0.10[b]	4.50 ± 0.08[c]	**−25.68 ± 0.07**	**−150.6 ± 0.2[b]**	−419
Pr(III)	1.01	4.56 ± 0.06[a] 4.58 ± 0.08[b]	4.57 ± 0.07[c]	**−26.10 ± 0.09**	**−10.3 ± 0.1[b]**	53
Nd(III)	0.99	4.58 ± 0.06[a] 4.63 ± 0.10[b]	4.61 ± 0.06[c]	**−26.25 ± 0.05**	**−141.0 ± 0.2[b]**	−385
Eu(III)	0.95	4.83 ± 0.05[a] 4.90 ± 0.15[b]	4.87 ± 0.10[c]	**−27.77 ± 0.06**	**−80.1 ± 0.1[b]**	−176
Gd(III)	0.94	4.83 ± 0.06[a] 4.89 ± 0.07[b]	4.86 ± 0.06[c]	**−27.74 ± 0.10**	**−95.3 ± 0.1[b]**	−227
Tb(III)	0.92	4.80 ± 0.05[a] 4.88 ± 0.09[b]	4.84 ± 0.07[c]	**−27.63 ± 0.11**	**−125.5 ± 0.1[b]**	−328
Ho(III)	0.89	4.74 ± 0.07[a] 4.77 ± 0.06[b]	4.76 ± 0.06[c]	**−27.17 ± 0.16**	**−189.9 ± 0.4[b]**	−546
Er(III)	0.88	4.74 ± 0.04[a] 4.75 ± 0.06[b]	4.75 ± 0.05[c]	−27.11 ± 0.13	−100.7 ± 0.2[b]	−247
Yb(III)	0.86	4.70 ± 0.05[a] 4.67 ± 0.05[b]	4.69 ± 0.05[c]	−26.77 ± 0.14	−43.4 ± 0.2[b]	−56

[a] UV spectrophotometric titration in acetonitrile at 298 K. [b] Microcalorimetric titration in acetonitrile at 298.15 K. [c] Average stability constant (log K_s) of UV spectrophotometric and microcalorimetric titrations.

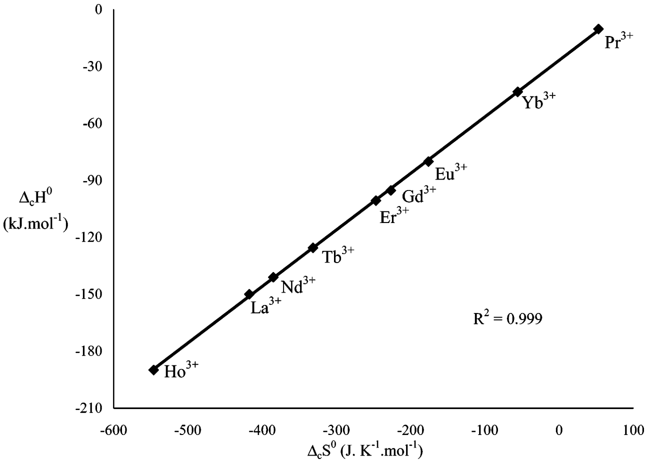

Figure 5. Standard entropy vs standard enthalpy of complexation of Ln^{3+} with **1b** in acetonitrile at 298.15 K.

at 298.15 K are also included in Table 3. These data are referred to the process represented by eq 1.

$$Ln^{3+}(s) + \mathbf{1b}(s) \rightarrow Ln^{3+}-\mathbf{1b}(s) \qquad (1)$$

Excellent agreement is found between the log K_s values obtained by the two different methods. An average log K_s value was used to calculate the $\Delta_cG°$ values reported in Table 3. Entropy values were calculated from the following relationship:

$$\Delta_cG° = \Delta_cH° - T\Delta_cS° \qquad (2)$$

In all cases, the standard deviation of the data is given. Judging from the stability constant values, derived from two independent methods, **1b** is unable to recognize selectively these cations in this solvent. Indeed, small variations are found in the complex stability of **1b** and these cations in this solvent. The large differences observed in the enthalpy and entropy for the different cations and this ligand lead to the conclusion that a striking enthalpy−entropy compensation[28] effect takes place as shown in Figure 5. The linear relationship observed has a slope of 299.6 K close to the experimental temperature of 298.15 K. The intercept of the fitted line is equal to $\Delta_cG° = -26 \pm 1$ kJ·mol^{-1}. This effect was previously found for other calix[4]arene derivatives and these cations in acetonitrile.[7] In addition, Choppin et al.[29] has also reported the absence of selectivity between chelating agents and lanthanide cations as a result of entropy−enthalpy compensation effects.

For **1c** and trivalent cations in MeCN, titration microcalorimetry and competitive potentiometry were used to determine the stability constants of these systems in this solvent. The ability of **1c** to interact with the silver cation in MeCN made it possible to use the potentiometric method using silver electrodes previously discussed.[30] This method is more versatile than calorimetry or indeed UV spectrophotometry, particularly when relatively stable complexes are formed. Thus, Table 4 lists log K_s values derived from potentiometry and microcalorimetry. Good agreement is found between the two sets of data. An average of these values is used to calculate the standard Gibbs energies of complexation, $\Delta_cG°$. Enthalpy (measured by microcalorimetry) and entropy data are also reported in Table 4.

Among the lanthanide cations, log K_s values vary from 4.70 (La^{3+}, average of two values) to 6.12 (Gd^{3+}, average of two values). Therefore, a difference of 1.4 log units is found between the weakest and the strongest complexes. This variation is quite close to that previously reported by our group[7] involving an analogue calix[4]arene amide derivative containing diisopropyl instead of diethyl groups attached to the amide nitrogen. However, it is important to stress that the strength of complexation of **1c** and lanthanide cations in acetonitrile is higher (by about 1 log unit) than that for the former ligand and these cations in this solvent. This is illustrated in Figure 6, where log K_s values for these two amide ligands and these cations in MeCN at 298.15 K are plotted against the ionic radii.[5,7,9] These data show the selective behavior of these ligands for the lanthanide cations and clearly demonstrate the increase in the strength of complexation in moving to **1c**.

This might be due to the replacement of the diisopropyl group in **1d**, by the diethyl group in **1c**, and can be attributed to the less bulky ethyl group relative to the isopropyl one, which reduces the steric effect in the hydrophilic cavity of **1c**, thus

TABLE 4. Thermodynamic Data for the Process of Complexation between Ln^{3+}−1c in Acetonitrile and *N,N*-dimethylformamide at 298.15 K

cation^{3+}	ionic radius^{5}	log K_s		$\Delta_c G°$ (kJ·mol^{-1})	$\Delta_c H°$ (kJ·mol^{-1})	$\Delta_c S°$ (J·K^{-1}·mol^{-1})
Y(III)	0.93	4.86 ± 0.02[a] 4.90 ± 0.04[b] 4.78 ± 0.05[c]	4.88 ± 0.03[d]	−27.85 ± 0.10	−10.7 ± 0.1[b]	57
Sc(III)	0.72	4.65 ± 0.03[a] 4.52 ± 0.02[b] 4.37 ± 0.02[c]	4.59 ± 0.02[d]	−26.14 ± 0.05	−36.2 ± 0.2[b]	−33
La(III)	1.06	4.80 ± 0.04[a] 4.60 ± 0.05[b] 4.53 ± 0.04[c]	4.70 ± 0.04[d]	−26.83 ± 0.16	−147.1 ± 0.4[b]	−403
Pr(III)	1.01	5.07 ± 0.03[a] 5.03 ± 0.02[b] 4.70 ± 0.02[c]	5.05 ± 0.02[d]	−28.83 ± 0.5	−43.3 ± 0.2	−48
Nd(III)	0.99	5.83 ± 0.03[a] 5.60 ± 0.05[b] 4.99 ± 0.05[c]	5.72 ± 0.04[d]	−32.60 ± 0.16	−51.8 ± 0.1	−64
Eu(III)	0.95	5.54 ± 0.04[a] 5.90 ± 0.06[b] 5.00 ± 0.02[c]	5.72 ± 0.05[d]	−33.62 ± 0.19	−89.7 ± 0.5[b]	−191
Gd(III)	0.94	6.13 ± 0.04[a] 6.11 ± 0.06[b] 5.12 ± 0.01[c]	6.12 ± 0.05[d]	−34.93 ± 0.19	−77.9 ± 0.1[b]	−144
Tb(III)	0.92	5.98 ± 0.02[a] 5.90 ± 0.04[b] 5.06 ± 0.03[c]	5.94 ± 0.03[d]	−33.90 ± 0.10	−91.2 ± 0.3[b]	−192
Ho(III)	0.89	5.68 ± 0.02[a] 5.69 ± 0.07[b] 4.97 ± 0.01[c]	5.69 ± 0.05[d]	−32.42 ± 0.23	−140.7 ± 0.1[b]	−363
Er(III)	0.88	5.70 ± 0.03[a] 5.62 ± 0.04[b] 4.92 ± 0.04[c]	5.66 ± 0.03[d]	−32.30 ± 0.10	−98.2 ± 0.2[b]	−220
Yb(III)	0.86	4.91 ± 0.04[a] 4.84 ± 0.03[b] 4.67 ± 0.05[c]	4.88 ± 0.03[d]	−26.77 ± 0.07	−200.6 ± 0.5[b]	−583

[a] Competitive potentiometric titration in acetonitrile at 298.15 K. [b] Microcalorimetric titration in acetonitrile at 298.15 K. [c] Competitive potenitometric titration in *N,N*-dimethylformamide at 298.15 K. [d] Average of the stability constant (log K_s) of competitive potentiometric and microcalorimetric titrations.

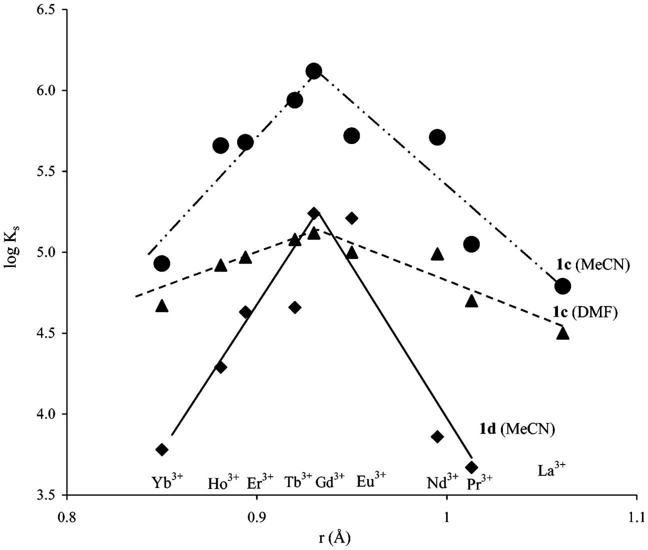

Figure 6. Comparison between log K_s values for Ln^{3+}−**1c** and Ln^{3+}−**1d** complexes vs the ionic radii of Ln^{3+} in acetonitrile and *N,N*-dimethylformamide at 298.15 K.

enabling this macrocycle to be more conformationally adjustable to embrace the cation than **1d**. However, this increase in stability with **1c** was associated with a decrease in enthalpy (less exothermic) accompanied by a gain in entropy for the first and middle Ln^{3+} series, with Eu^{3+} being an exception since it showed higher enthalpy values, relative to **1d**. Moreover, for the last three Ln^{3+} cations (Ho^{3+}, Er^{3+}, and Yb^{3+}) the complexation process is enthalpically controlled (exothermic) with a greater loss of entropy with respect to **1d** and these cations in MeCN at 298.15 K.

It appears that, along the lanthanide series investigated, the interaction of Yb^{3+}, Eu^{3+}, and Pr^{3+} with **1c** is characterized by a higher exothermicity (more enthalpically favored) coupled by a greater loss in entropy as compared to **1b**. These findings indicate that, upon complexation, the ligand binding process ($\Delta_c H° < 0/\Delta_c S° < 0$) predominates over the cation desolvation process ($\Delta_c H° > 0/\Delta_c S° > 0$). For the remaining cations in the lanthanide series, less exothermicity accompanied by a gain in entropy is observed, thus suggesting that upon complexation the cation, ligand, or complex desolvation predominates over the ligand binding energy. The different thermodynamic behavior of these three metal cations and **1c** falling in the heavy (Yb^{3+}), middle (Eu^{3+}), and light (Pr^{3+}) categories along the lanthanide series may lead to the selectivity peak observed. Thus, plots of $\Delta_c H°$ for the **1b**−Ln^{3+} and **1c**−Ln^{3+} complexes vs ionic radii (Figure 7) are mirrored by the plots of their corresponding $\Delta_c S°$ values for these systems vs ionic radii (Figure 8). From these figures, it can be noted that the complexes of Yb^{3+}, Eu^{3+}, and Pr^{3+} with **1b** form the three peaks of a "W".

The medium effect on the stability of these complexes was assessed by the determination of log K_s values for **1c** with trivalent cations in DMF. These data obtained by competitive potentiometry are shown in Table 4. Cation size dependence on log K_s values in DMF is also shown in Figure 6. DMF, being

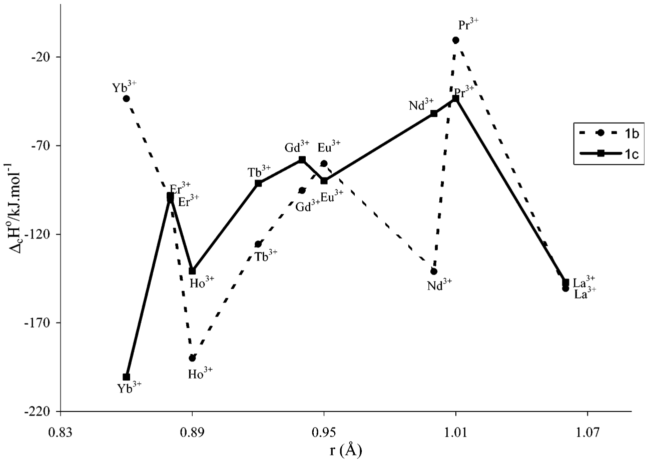

Figure 7. Comparison between the values of $\Delta_cH°$ for Ln^{3+}−**1b** and Ln^{3+}−**1c** complexes vs the ionic radii of Ln^{3+} in acetonitrile at 298.15 K.

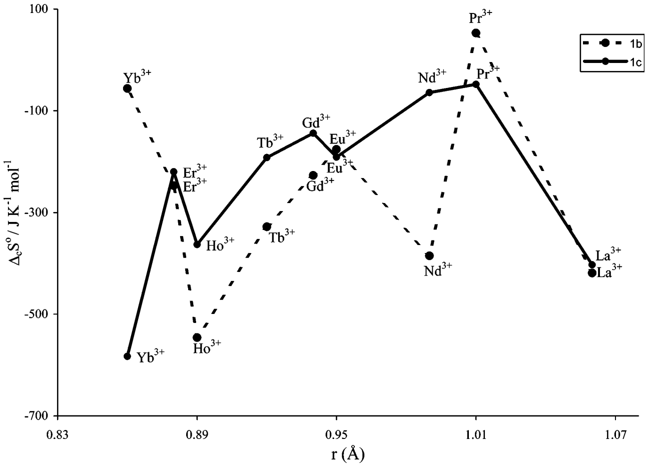

Figure 8. Comparison between the values of $\Delta_cS°$ for Ln^{3+}−**1b** and Ln^{3+}−**1c** complexes vs the ionic radii of Ln^{3+} in acetonitrile at 298.15 K.

a protophilic dipolar aprotic solvent, is a good cation solvator, and therefore, the complex stability in this solvent decreases.[31] It should be emphasized that although the selective behavior of **1c** to lanthanide(III) cations is maintained, it is reduced as shown by the more flattened selectivity peak observed in Figure 6. Whether this is mainly attributed to the free cation, ligand, and/or metal ion complex remains to be investigated.

Final Conclusions

From the above discussion the following conclusions can be drawn.

(i) Among these macrocycles the σ-donating ability of the carbonyl oxygens increases in the sequence **1a** < **1b** < **1c**, and therefore, their basicity increases. As a result the strongest complexes are formed between **1c** and trivalent cations in MeCN and DMF. In all cases 1:1 complexes are formed as shown by ^{1}H NMR and conductance measurements. This is further corroborated by the fact that the model used for the calculation of thermodynamic data (1:1 metal cation:ligand ratio) fits the experimental data. In all cases, the complexation process is enthalpically controlled since a loss of entropy is observed upon interaction of these ligands and these cations in these solvents. The lack of selectivity of **1b** and trivalent cations in MeCN at 298.15 K is due to a remarkable enthalpy−entropy compensation effect. Interaction between **1a** and trivalent cations in MeCN was found to be weak.

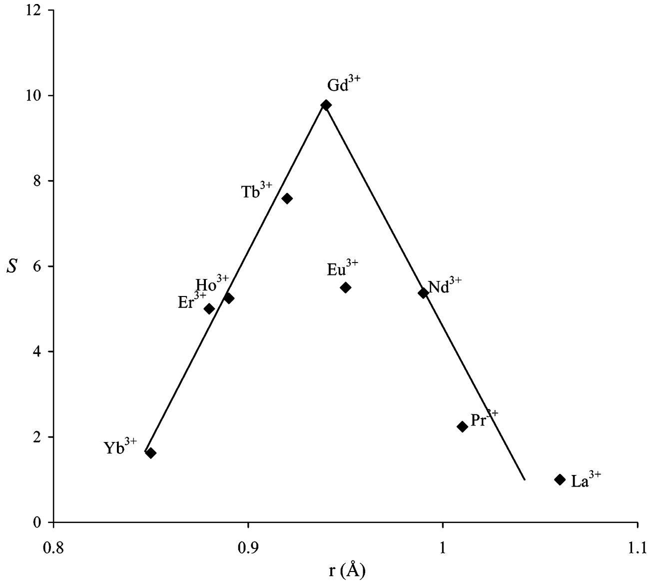

Figure 9. Selectivity factor (S) of Ln^{3+}−**1c** complexes in acetonitrile relative to *N*,*N*-dimethylformamide at 298.15 K vs the ionic radii of Ln^{3+}.

(ii) **1c** is selective for trivalent cations in MeCN and DMF at 298.15 K. In this paper we demonstrate that the nature of the alkyl groups attached to the amide nitrogens and the solvent have a considerable effect on complex stability. As far as the former is concerned, in moving from **1d** to **1c**, a considerable increase in stability is found. In fact, for a given trivalent cation, the latter ligand is more selective than the former by factors of 1, 7, 24, 72, 3, 8, 19, 11, 22, and 13 for Y^{3+}, Sc^{3+}, Pr^{3+}, Nd^{3+}, Eu^{3+}, Gd^{3+}, Tb^{3+}, Ho^{3+}, Er^{3+}, and Yb^{3+} respectively.

As far as the medium effect is concerned, the selective behavior of **1c** is more pronounced in MeCN than in DMF. Thus, in Figure 9 the selectivity factor for each cation in these two solvents ($S = K_s(\mathrm{MeCN})/K_s(\mathrm{DMF})$) is plotted against the ionic radii of the cation. These data show that in moving from DMF to MeCN there is an increase in S from Yb^{3+} to Gd^{3+} and then a decrease from the latter to La^{3+}. The various factors controlling the selectivity enhancement observed in MeCN relative to DMF are under study.[32]

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