



## Lanthanide Cation Binding Properties of Homooxacalixarene Diethylamide Derivatives

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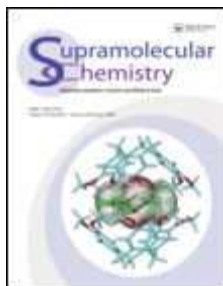
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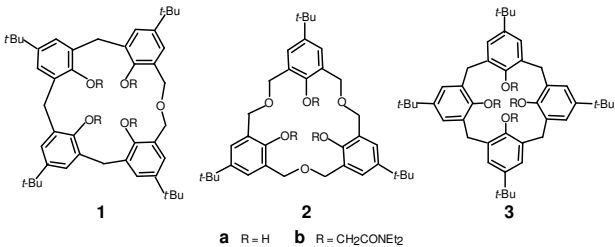


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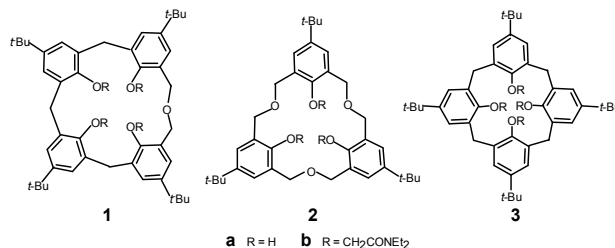


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# Lanthanide Cation Binding Properties of Homooxacalixarene Diethylamide Derivatives

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## Abstract

The binding properties of two homooxacalixarene diethylamides (**1b** and **2b**) derived from *p*-*tert*-butyldihomooxacalix[4]arene and *p*-*tert*-butylhexahomotrioxacalix[3]arene respectively, in the cone conformation, for lanthanide cations were investigated. These properties were assessed by extraction studies of the metal picrates from water into dichloromethane and stability constant measurements in methanol, using spectrophotometric and potentiometric techniques. Microcalorimetric studies of  $\text{La}^{3+}$ ,  $\text{Pr}^{3+}$ ,  $\text{Eu}^{3+}$  and  $\text{Gd}^{3+}$  complexes in the same solvent were also performed. Proton NMR titrations with the representative lanthanides  $\text{La}^{3+}$ ,  $\text{Eu}^{3+}$  and  $\text{Yb}^{3+}$  were also carried out to establish the sites of interaction of the ligands with the cations. The analogous derivative (**3b**) of *p*-*tert*-butylcalix[4]arene was also studied and the results of the three compounds are compared. Diethylamide **1b** is the strongest binder, showing some preference for the light lanthanides in extraction, but exhibiting practically no selectivity in complexation. **1b** displays the highest stability constant values ever found with this ligand ( $\log \beta = 8.6 - 9.2$ ). In contrast, **2b** shows lower extraction and stability constant values, but it is a more selective ligand, showing a clearer preference for the light lanthanides. Diethylamide **3b** exhibits a similar behaviour to that of its analogous **1b**. Proton NMR titrations confirm the formation of 1:1 complexes between the amides and the cations studied, also indicating that they should be located inside the cavity defined by the phenoxy and the carbonyl oxygen atoms.

**Keywords:** Dihomooxacalix[4]arene; Hexahomotrioxacalix[3]arene; Diethylamide derivative; Lanthanide cation binding; Proton NMR titration.

## Introduction

More than 30 years after the beginning of modern calixarene chemistry, calixarenes (*1-3*) continue attracting much attention as ion receptors and carriers in host-guest chemistry. The parent compounds are readily available and can be further functionalised on the upper and lower rims to give a large variety of derivatives.

In particular, the ability of carbonyl containing substituents on the lower rim of calixarenes to bind metal ions, predominantly alkali and alkaline earth (*4*), but also transition and heavy metal cations (*5*), has been largely studied. Besides these mono and divalent cations, research work with trivalent cations, namely lanthanides (*6, 7*), has also been increasingly reported. The growing interest in these elements is mainly due to their use in materials for catalysis, optics, electronics, in luminescent probes, in biology and in medicine as contrast agents for magnetic resonance imaging. The study of the interactions between calixarenes and lanthanides is also motivated by the treatment of radioactive wastes, which requires the extraction of lanthanides and actinides from acidic effluents, followed by their separation before the disposal or the transmutation of the actinides into short-lived radionuclides.

Lanthanide ions, being hard Lewis acids (*8*), show strong affinity towards hard oxygen donor atoms. Thus, it is expected that calixarenes containing such donor atoms are potential receptors for those cations. Phosphorylated calix[4]arenes, bearing carbamoylmethylphosphine oxides (CMPO) (*6a, b, 9, 10*) moieties on the upper and lower rims or phosphine oxide (*11, 12*), as well as calix[4]arene derivatives with lower rim carbonyl containing substituents, such as esters (*13*), carboxylic acids (*13-15*) and amides (*16-18*), have been used as extracting agents for lanthanide ions. Also the larger and more flexible calix[6]- (*18, 19*) and calix[8]arenes (*18-20*) have been investigated, since lanthanide cations require high

coordination numbers (8 or 9) and, therefore, more donor sites can be favourable to their complexation.

Both dihomooxacalix[4]arene and hexahomotrioxacalix[3]arene, calixarene analogues in which one or all CH<sub>2</sub> bridges are replaced by CH<sub>2</sub>OCH<sub>2</sub> groups respectively, are more flexible molecules than calix[4]arenes, but still possess a cone conformation, the most appropriate for complexation. In the course of the studies of binding and transport properties of homooxacalixarenes bearing carbonyl groups at the lower rim, namely the amide function (21, 22), towards alkali, alkaline earth, transition and heavy metal cations, we have recently extended our research into lanthanide ions (23).

This paper reports the binding properties of two diethylamides, **1b** (24) and **2b** (25), derivatives of *p*-*tert*-butyldihomooxacalix[4]arene (**1a**) and of *p*-*tert*-butylhexahomotrioxacalix[3]arene (**2a**) respectively (Figure 1), in the cone conformation, towards lanthanide cations (La<sup>3+</sup>, Ce<sup>3+</sup>, Pr<sup>3+</sup>, Nd<sup>3+</sup>, Sm<sup>3+</sup>, Eu<sup>3+</sup>, Gd<sup>3+</sup>, Dy<sup>3+</sup>, Er<sup>3+</sup> and Yb<sup>3+</sup>). Extraction studies of metal picrates from an aqueous solution into dichloromethane and stability constant measurements in methanol based on UV absorption spectrophotometry and competitive potentiometry were performed. Thermodynamic parameters of La<sup>3+</sup>, Pr<sup>3+</sup>, Eu<sup>3+</sup> and Gd<sup>3+</sup> complexation were determined by microcalorimetric titrations. The affinity of the ligands for La<sup>3+</sup>, Eu<sup>3+</sup> and Yb<sup>3+</sup> cations has also been investigated by proton NMR spectrometry, mainly to establish the binding sites. Those three cations were chosen as representatives of the light, middle and heavy categories of the lanthanide series. The diethylamide (**3b**) (26) derivative of *p*-*tert*-butylcalix[4]arene (**3a**) is also studied in this work and the results of the three derivatives are compared and discussed in terms of the size and conformational effects of the macrocycles.



## Results and discussion

### Extraction studies

The ionophoric properties of diethylamides **1b**, **2b** and **3b**, all in the cone conformation, towards lanthanide cations were first evaluated by the standard picrate method (27). The results, expressed as percentages of cation extracted (% *E*), are collected in Table 1.

The data reveal that amide **1b** displays very high extraction levels for all the cations (% *E* ranges from 41 to 76). These values are significantly higher (more than double) than those obtained for amide **2b** (% *E* ranges from 13 to 34), the maximum difference being observed in the cases of  $\text{Er}^{3+}$  and  $\text{Dy}^{3+}$  cations. This behaviour was expected as lanthanides require high coordination numbers (8 or 9) and **2b** possesses only three amide groups, and consequently only six donating sites can surround the cations, compared to the eight sites of tetraamide **1b**. However, **2b** is a more selective extractant agent than **1b** (for example,  $S_{\text{Pr}^{3+}/\text{Yb}^{3+}} = 2.6$  and 1.8, respectively, where selectivity  $S = \% E_{\text{M1}^{3+}} / \% E_{\text{M2}^{3+}}$ ). Derivative **1b** also shows a much higher extraction percentage than that of the amide **3b** (% *E* ranges from 12 to 24). Moreover, compared to the extraction percentages of europium picrate (the only data found in the literature) (4a) with the larger calix[5]- (24% *E*) and calix[6]arene (39% *E*) amide analogues, we verify that **1b** still displays the highest values.

Both amides **1b** and **2b** show similar extraction profiles. They do not display any peak selectivity among the cations, but they clearly discriminate between the light and the heavy lanthanides. The former cations (from  $\text{La}^{3+}$  to  $\text{Eu}^{3+}$ ) are preferred over the latter (with exception of **1b** with  $\text{Dy}^{3+}$ ), and among those a very slight selectivity can be observed for  $\text{Pr}^{3+}$ ,  $\text{Nd}^{3+}$  and  $\text{Ce}^{3+}$  with both derivatives, and also for  $\text{Eu}^{3+}$  with **1b**. Despite the small variations among the ionic radii of the lanthanide ions (0.16 Å from  $\text{La}^{3+}$  to  $\text{Yb}^{3+}$ ), the relative larger size of those cations may account for these differences, as both derivatives have been

showing a stronger affinity for the larger cations (21, 22). This extraction trend is, however, the opposite of that found by us for the corresponding ketone derivatives (23). In the case of amide **3b**, the extraction profile is slightly different. This derivative does not display any peak of selectivity either, but shows preference for the middle lanthanides, as  $\text{Eu}^{3+}$ ,  $\text{Sm}^{3+}$  and  $\text{Dy}^{3+}$ .

### Complexation studies

The complexation of some representative lanthanide cations ( $\text{La}^{3+}$ ,  $\text{Pr}^{3+}$ ,  $\text{Eu}^{3+}$ ,  $\text{Gd}^{3+}$  and  $\text{Yb}^{3+}$ ) was followed by UV absorption spectrophotometry and/or competitive potentiometry for ligands **1b**, **2b** and **3b** in methanol. The logarithms of the stability constants  $\beta$  of the 1:1 complexes formed are given in Table 2. For all these cations except  $\text{Yb}^{3+}$ , the complexation thermodynamic parameters were determined by microcalorimetry with ligands **1b** and **2b** in the same solvent. These data are collected in Table 3.

The first results were obtained with the lanthanide chlorides by spectrophotometry in the presence of tetraethylammonium chloride as the supporting electrolyte. Very significant spectral changes were observed in the spectrum of **1b** during its titration against the metal salts, until the metal to ligand concentration ratio reaches 1, indicating the formation of very stable 1:1 complexes (Figure 2). With the hexahomotrioxacalix[3]arene **2b**, much weaker spectral variations could be noticed. In contrast to **1b**, for which only a lower limit could be estimated ( $\log \beta \geq 7$ ), the interpretation of the experimental data for **2b** led to reliable stability constants for the 1:1 complexes (Table 2).

As the stability constants obtained with **1b** and metal chlorides were too high, and at the limits of the experimental method, it was decided to follow the complexation of lanthanide nitrates in the presence of  $\text{Et}_4\text{NNO}_3$  as the supporting electrolyte. Previous studies on phosphorylated calixarene derivatives showed an important decrease of the stability

constants in such a more co-ordinating medium (10). Although much lower values were found with **2b** (for instance the stability of the lanthanum complex drops from 5.5 to 2.2 log units on changing the counterion from chloride to nitrate), the stability constants remained, however, very high for the complexes of derivative **1b**, with values ranging between 6.2 and 5.5 log units.

In order to better assess the high stability constants of the complexes with **1b**, potentiometric experiments based on a competition with the  $\text{Ag}^+$  cation were then performed with lanthanide trifluoromethanesulfonates (triflates) in the presence of  $\text{Et}_4\text{NClO}_4$  as the supporting electrolyte. The stability constant of the 1:1  $\text{Ag}^+$  complex has been re-evaluated and the result ( $\log \beta = 7.16$ ) found is in excellent agreement with the value published earlier (21). For comparison the stability constants of the 1:1 complexes with *p*-tert-butylcalix[4]arene tetra(diethyl)amide **3b** were also determined for  $\text{Ag}^+$  and for the selection of lanthanides studied. The values for  $\text{Ag}^+$  ( $\log \beta = 7.56$ ) and for  $\text{Pr}^{3+}$ ,  $\text{Eu}^{3+}$  and  $\text{Yb}^{3+}$  complexes (Table 2) are consistent with those published earlier (28, 4a).

In order to get a better insight into the origin of the stability of these complexes, the complexation of  $\text{La}^{3+}$ ,  $\text{Pr}^{3+}$ ,  $\text{Eu}^{3+}$  and  $\text{Gd}^{3+}$  triflates and of  $\text{La}^{3+}$  nitrate was followed by microcalorimetric experiments, which allowed the determination of the complexation thermodynamic parameters.  $\text{Yb}^{3+}$  triflate was not soluble enough to obtain significant heat effects during the titrations of the ligands with this cation. Therefore, no data could be derived in this case. With **1b**, the thermograms were simple, showing exothermic heat signals until a 1:1 stoichiometry was reached, as illustrated in the case of  $\text{Gd}^{3+}$  (Figure 3). They are consistent with the formation of very stable 1:1 complexes, in agreement with the spectrophotometric and potentiometric results. The enthalpies of complexation,  $\Delta H$ , determined from the slopes of the cumulative heat effects versus the number of moles of reactant added, and the corresponding entropies of complexation,  $\Delta S$ , calculated from the

Gibbs energy derived from the stability constants obtained from potentiometry are listed in Table 3. With **2b**, the thermograms are quite different showing endothermic effects, as for example for  $\text{Gd}^{3+}$  (Figure 4). In this case, both the logarithm of the stability constants and the enthalpy of complexation could be refined simultaneously (Table 3). The stability constants were found to be slightly higher than those determined by spectrophotometry with chloride counterions. With **3b** and all the lanthanides studied, the thermograms were more complex: they started with exothermic signals, becoming endothermic from a metal to ligand concentration ratio of 0.7 and exothermic again, corresponding to the dilution effect, after the 1:1 stoichiometry. They are certainly consistent with several complexation processes, including the formation of a 1:1 complex as with the other ligands studied. They may also show, at some extent, micro-precipitation, which could be the reason why they could not be interpreted.

The main conclusions are the following:

(i) The dihomooxa derivative **1b** shows a higher affinity for lanthanides than its hexahomotrioxa counterpart **2b**. For instance, the  $\text{Eu}^{3+}$  complex is at least 2.3 log units higher with **1b** than with **2b** with chloride counterions and 4 log units higher with nitrate counterions. This is consistent with the remarkable extraction efficiency of **1b** as compared with **2b**. In contrast, there is no great difference in stability between the complexes with **1b** and its calix[4]arene counterpart **3b**,  $\log \beta$  values being in the ranges 9.2 – 8.6 and 8.9 – 8.2, respectively.

(ii) The stability of the complexes is strongly dependent on the medium. As expected from the coordinating properties of the anions towards lanthanides in methanol (29), the complexes are less stable in the presence of nitrate ions than in the presence of the less coordinating

chloride and especially perchlorate / triflate anions. For instance,  $\log \beta$  of the  $\text{Eu}^{3+}$  complex with **2b** decreases from 4.7 to 2.08 on going from the chlorides to the nitrates. Similar observations have been made with phosphorylated calixarenes, which have been ascribed to the strong ability of anions such as nitrates, to interact with the lanthanides and to compete with the ligands for their complexation (10).

(iii) The influence of the lanthanidic contraction on the complex stability appears to be different according to the ligands. Whereas an irregular variation of stability prevails along the series with **1b** and **3b**, showing no specific trend, there is a clear decrease of the stability of the complexes with **2b**, for instance from 5.5 log units for the  $\text{La}^{3+}$  complex to 3.4 log units for the  $\text{Yb}^{3+}$  complex, when chloride is the counterion. Although to a lesser extent with **1b** and **3b**,  $\text{Yb}^{3+}$  seems to be the least complexed cation by the three ligands. These trends contrast with those observed for classical non macrocyclic chelating agents (as for example aminopolycarboxylic ligands) (30) where the stability of lanthanide complexes generally increases along the series with the charge density on the cation. Obviously, other factors like the size and the flexibility of the ligands, may account for these differences.

(iv) With **1b**, the stabilization of the complexes is driven by the enthalpy and the entropy changes which vary irregularly from  $\text{La}^{3+}$  to  $\text{Gd}^{3+}$ . The former are clearly negative, ranging from  $-24.78$  to  $-31.77 \text{ kJ mol}^{-1}$ , and the latter clearly positive, ranging from  $21$  to  $25.78 \text{ kJ mol}^{-1}$ , being hence both favourable. The situation is quite different with **2b**, since the stabilization is only due to favourable entropy terms, which are more or less constant ( $73.4 - 71 \text{ kJ mol}^{-1}$ ) with the first three cations and increases to  $81.7 \text{ kJ mol}^{-1}$  with  $\text{Gd}^{3+}$ . In contrast, the enthalpy contribution is positive and hence unfavourable, especially with  $\text{Gd}^{3+}$  ( $\Delta H = 50.8 \text{ kJ mol}^{-1}$ ). In fact, with both ligands, the entropic terms are always positive and favourable.

This is certainly due to the importance of the solvation of the lanthanides. Another factor, which cannot be neglected, is the ligand solvation. With **2b**, possessing in its macrocyclic skeleton three ethereal oxygen atoms, solvation is expected to be stronger than with **1b**. This can explain, at least partly, both the low enthalpy and the high entropy terms observed with the former ligand. In the absence of reliable data in methanol for the calix[4]arene counterpart **3b**, these results can be compared to previous data concerning the complexation of alkaline earth cations by **3b** in the same solvent. With these systems involving multicharged cations, the complexation process was also entropically controlled (31).

Changing the counter ion from triflate to nitrate has also an influence on  $\Delta H$  and  $T\Delta S$ , as seen for the complexation of lanthanum with **1b** and **2b**, which is characterized by slightly more favourable or less unfavourable enthalpic terms and to less positive entropic contributions. These results are consistent with the nitrate anions still interacting with the cation in the complexes.

### Proton NMR studies

To obtain further information on the cation binding behaviour of diethylamides **1b**, **2b** and **3b**, specifically concerning the binding sites, proton NMR titrations were performed in  $\text{CDCl}_3/\text{CD}_3\text{OD}$ . The cations studied were  $\text{La}^{3+}$ ,  $\text{Eu}^{3+}$  and  $\text{Yb}^{3+}$ . Variable amounts of the salts were added to the ligands and the proton spectra recorded after each addition.

Different situations were found after the addition of the salts to the ligands. The three amides exhibit similar behaviours towards  $\text{La}^{3+}$ . These titrations show that with  $[\text{salt}]/[\text{ligand}]$  ratios lower than one, both signals of the complexed and uncomplexed ligands are present in the spectra, indicating that on the NMR time scale the exchange rate between the two species is slow at room temperature. This behaviour reflects the high affinity of these ligands towards

La<sup>3+</sup> as previously observed. Upon reaching 1:1 ratios, all the signals for the free ligands disappear and those of the complexed ligands remain unaltered after subsequent addition of the salt, indicating a 1:1 metal-to-ligand stoichiometry. In the case of ligand **1b**, besides the 1:1 complex, another set of sharp signals with lower intensity can be seen in the spectra, from the addition of the first aliquot of salt (Figure 5). This possibly reflects a 1:2 metal-to-ligand stoichiometry for the second complex (B), since the intensity of B peaks decreases as the addition of the salt proceeds. Similar situations have already been observed by us before (32, 33). In order to confirm the stoichiometry of these complexes, a Job plot based on <sup>1</sup>H NMR data was carried out. The Job plot shown in Figure 6 clearly confirms the formation of a 1:1 metal-to-ligand complex, but no unambiguous stoichiometry can be established from the curve for the weaker complex (B), due to the predominance of complex A (34). Complex B shows a plateau rather than a maximum between 0.5 and 0.6 mole fraction of **1b**, the same situation found by us before with two ketone derivative analogues and Ca<sup>2+</sup> and Sr<sup>2+</sup> cations. In contrast, titrations of diethylamides **1b**, **2b** and **3b** with Eu<sup>3+</sup> and mainly Yb<sup>3+</sup> produce broad and distorted proton signals, which are shifted toward high and low fields. This behaviour is more evident for derivatives **1b** and **3b**, and the shifts observed cover a range greater than 20 ppm. This is consistent with the knowledge that the binding of paramagnetic metal ions, such as Eu<sup>3+</sup> and Yb<sup>3+</sup>, causes enhanced shift and relaxation effects on the resonances of the nuclei of the ligands (6c). The results indicate that complexation occurs between the ligands and these cations, and are in agreement with those obtained by spectrophotometry / potentiometry in the present study.

Proton NMR data of the free and complexed ligands are collected in Table 4. The complete interpretation of the spectrum for compound **1b** required an additional COSY spectrum. However, in the case of the weaker complex (B), full proton assignment was not possible due to overlapping of signals arising from both complexed species. Complexation of



La<sup>3+</sup> affects all the proton chemical shifts in ligands **1b**, **2b** and **3b**. In the case of Eu<sup>3+</sup> and Yb<sup>3+</sup> the broad and distorted signals obtained, as already mentioned, prevented a quantitative analysis of the data.

The largest chemical shift changes are recorded for the bridging axial methylene protons (ArCH<sub>2</sub>Ar) and the oxygen bridge equatorial methylene protons (CH<sub>2</sub>OCH<sub>2</sub>), in the case of **2b**, which move upfield, and by the aromatic protons and the methylene protons of the OCH<sub>2</sub>CO groups, which move downfield. As observed for other calixarenes, the variation in chemical shift experienced by the equatorial methylene protons (ArCH<sub>2</sub>Ar) is downfield and smaller than that of the axial protons, but in the present case it is still very high ( $\Delta\delta = 0.52$  and  $0.53$  ppm for **1b** and  $0.60$  ppm for **3b**). The CH<sub>2</sub>OCH<sub>2</sub> resonances behave differently, as previously reported (21-23). The equatorial methylene protons of the oxygen bridge move upfield and experience larger shift variations than the axial ones. These results suggest that the oxygen bridge conformation changes significantly upon complexation, with the equatorial protons undergoing a higher shielding effect. The smallest variations are observed for the protons of the N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub> and *tert*-butyl groups.

A closer examination of the spectral changes upon complexation indicates that the differences in the chemical shifts between the axial and the equatorial protons of the ArCH<sub>2</sub>Ar bridges in ligands **1b** and **3b** ( $\Delta\delta = 1.64, 1.77$  ppm for **1b** and  $2.10$  ppm for **3b**) decrease ( $\Delta\delta = 0.46, 0.39$  ppm for **1b** and  $0.51$  ppm for **3b**), being closer to  $0.5$  ppm (35). This suggests that the free ligands depart from a distorted cone conformation and adopt a flattened cone conformation after complexation, with their pendant arms moving closer together. If Gutsche's criterion is also applicable to the CH<sub>2</sub>OCH<sub>2</sub> bridges, it indicates that ligand **2b** is much more flattened ( $\Delta\delta = 0.32$  ppm) than **1b** and **3b**, and stands up when the cation enters into the ionophoric cavity ( $\Delta\delta = 0.74$  ppm).



The deshielding effect observed for the aromatic protons indicates the involvement of the phenolic oxygens in complexation, as reported previously (36). The largest shift changes shown by the protons adjacent to the oxygen donor atoms can be explained in terms of variations of both shielding and deshielding effects of the aromatic rings and carbonyl groups upon cation binding to those donor atoms. Therefore, this suggests that the cation must be inside the cavity defined by the phenoxy and carbonyl oxygen atoms and bound through metal-oxygen interactions.

## Conclusions

Extraction studies from an aqueous solution into  $\text{CH}_2\text{Cl}_2$  and stability constant measurements in methanol have shown that diethylamide **1b** is a very strong binder for lanthanides, showing high extraction percentages and the highest stability constant values ever found with this ligand ( $\log \beta = 8.6 - 9.2$ ). It displays some preference for the light lanthanides (from  $\text{La}^{3+}$  to  $\text{Eu}^{3+}$ ) in extraction, but it does not noticeably discriminate between them (from  $\text{La}^{3+}$  to  $\text{Yb}^{3+}$ ) in complexation. In the case of diethylamide **2b**, the data showed that it is a weaker extractant and exhibits lower  $\log \beta$  values, but it is a more selective ligand, showing clearly a positive discrimination for the light lanthanides. The weaker binding power of **2b** may be due to its lack of donating sites compared to **1b**, as lanthanide cations require high coordination numbers. Diethylamide **3b** exhibits a similar behaviour to that of its analogous **1b**, at least in complexation. With **1b** the complexation process of all the cations is enthalpically and entropically stabilised, since the enthalpy changes are clearly negative, while the entropy changes are positive. In contrast, the complexation process with **2b** is governed by the entropy changes only. Proton NMR titrations corroborated the formation of 1:1 complexes between all the amides and  $\text{La}^{3+}$  cation, also indicating that the cation should be encapsulated into the

cavity defined by the phenoxy and the carbonyl oxygen atoms. In the case of complexation of **1b** with  $\text{La}^{3+}$ , besides the 1:1 complex, minor amounts of another complex with a different ligand-to-metal stoichiometry was formed.

## Experimental

### Extraction studies

Equal volumes (5 mL) of aqueous solutions of metal picrates ( $2.5 \times 10^{-4}$  M) and solutions of the calixarenes ( $2.5 \times 10^{-4}$  M) in  $\text{CH}_2\text{Cl}_2$  were vigorously shaken for 2 min, and then thermostated in a water bath with mechanical stirring at 20 °C overnight. After complete phase separation, the concentration of picrate ion in the aqueous phase was determined spectrophotometrically ( $\lambda_{\text{max}} = 354$  nm). For each cation-calixarene system the absorbance measurements were repeated at least four times. Blank experiments showed negligible picrate extraction in the absence of a calixarene. The details of the metal picrate preparation have already been described (23).

### Determination of stability constants

UV absorption spectrophotometric titrations were carried out to obtain the stability constants ( $\log \beta$ ) of the complexes formed between the lanthanide chlorides (and in some cases lanthanide nitrates) and the two ligands **1b** and **2b**. All the experiments were performed in methanol at 25 °C in the presence of  $\text{Et}_4\text{NCl}$  as the supporting electrolyte. The detail of the procedure has been published previously (28). The ligand concentrations were in the range  $6.4 \times 10^{-5} - 5.7 \times 10^{-4}$  M and the final cation to ligand concentration ratios were in the range 1.5 – 10, depending on the strength of the complexes. The measurements were treated by the

program Specfit (37) to give the stoichiometry and the stability constants of the complexes. For very stable complexes ( $\log \beta \geq 7$ ), *i.e.* with ligands **1b** and **3b**, potentiometric titrations based on a competition with  $\text{Ag}^+$  as auxiliary cation, were performed as already described (28). The  $\text{Ag}^+$  concentration was typically around  $7.5 \times 10^{-4}$  M. Similar lanthanide concentrations were used except for  $\text{Yb}^{3+}$  solutions, which were about  $1.6 \times 10^{-4}$  M. The data were treated using the program SIRKO (38).

The lanthanide (lanthanum, praseodymium, europium, gadolinium and ytterbium) salts used for spectrophotometric measurements were chlorides and in some cases (lanthanum, europium and ytterbium) also nitrates. They were all purchased from Alfa Aesar (99.99 %). Tetraethylammonium chloride (Fluka, purum,  $\geq 98$  %) and nitrate (Acros Organics, 99 %) supporting electrolyte were used without further purification. The metal salts used for potentiometric measurements were the lanthanide and silver trifluoromethanesulfonates (Alfa Aesar, min 98 %). In these cases, tetraethylammonium perchlorate (Fluka, purum,  $\geq 99$  %) was used as the supporting electrolyte. All these salts were dried under vacuum at ambient temperature during 48 hours before use. The concentration of the lanthanide stock solutions (*ca.*  $10^{-2}$  M) was standardized by complexometry with EDTA using xylenol orange as coloured indicator (39). The concentration of  $\text{Ag}^+$  solutions was determined by potentiometry with addition of NaCl. Methanol (Sigma Aldrich, Chromasolv, water content max 0.03 %) was used without further purification.

### Microcalorimetric titrations

Microcalorimetric experiments were performed using a 2277 Thermal Activity Monitor Microcalorimeter (Thermometric). Titrations were carried out at 25 °C on 2.5 mL of the ligand solution in methanol of concentrations ranging from  $8.0 \times 10^{-5}$  to  $4.0 \times 10^{-3}$  M, using a

4 mL glass cell. The heats of complexation were measured after addition of  $17 \times 15 \mu\text{L}$  aliquots of *ca.*  $6.0 \times 10^{-3}$  M lanthanide triflate solutions or *ca.*  $5.0 \times 10^{-2}$  M lanthanum nitrate solutions in the same solvent and then corrected for the heat of dilution of the metal salt determined in separate titrations without the ligands. Chemical calibration of the calorimeter was made by determination of the complexation enthalpy of  $\text{Rb}^+$  with 18C6 in methanol as recommended (40). With ligands **1b** and **3b**, the stability constants ( $\log \beta \geq 7$ ) were high enough to consider that the complexes formed completely after each addition of metal ion. In this cases, the complexation enthalpy,  $\Delta H$ , was obtained from the slope of the linear plots of the corrected cumulated heats exchanged versus the number of moles of metal added until the 1:1 stoichiometry. With ligand **2b**, which forms less stable complexes with all the cations studied except  $\text{La}^{3+}$ ,  $\log \beta$  and  $\Delta H$  were calculated simultaneously using the program DIGITAM version 4.1 (41). The corresponding complexation entropies were then calculated from the equations  $\Delta G = \Delta H - T\Delta S$  and  $\Delta G = -RT \ln \beta$ , knowing  $\beta$  from spectrophotometry.

### Proton NMR experiments

Several aliquots (up to 2–3 equiv) of the salt solutions (0.25 M) in  $\text{CD}_3\text{OD}$  were added to  $\text{CDCl}_3$  solutions ( $5 \times 10^{-3}$  M) of the ligands directly in the NMR tube. The salts used were La, Eu and Yb triflates. Due to the low solubility of Eu triflate in MeOH, it was necessary to decrease the concentration of the ligand ( $2.5 \times 10^{-4}$  M) and of the salt ( $4.17 \times 10^{-3}$  M). The spectra were recorded on a Bruker Avance III 500 Spectrometer after each addition of the salts. The temperature of the NMR probe was kept constant at 22 °C. Job's method was performed for diethylamide **1b** and La triflate. The total concentration was maintained at  $1 \times 10^{-2}$  M in  $\text{CDCl}_3\text{-CD}_3\text{OD}$  (9:1). The COSY spectrum was the result of 32 transients per increment, in a total of 256.

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**Table 1.** Percentage extraction of lanthanide picrates into CH<sub>2</sub>Cl<sub>2</sub> at 20 °C<sup>a</sup>

	La <sup>3+</sup>	Ce <sup>3+</sup>	Pr <sup>3+</sup>	Nd <sup>3+</sup>	Sm <sup>3+</sup>	Eu <sup>3+</sup>	Gd <sup>3+</sup>	Dy <sup>3+</sup>	Er <sup>3+</sup>	Yb <sup>3+</sup>
Ionic radius <sup>b</sup> /Å	1.03	1.01	0.99	0.98	0.96	0.95	0.94	0.91	0.89	0.87
<b>1b</b>	71	74	76	75	69	75	47	67	57	41
<b>2b</b>	28	34	34	34	31	30	17	18	13	13
<b>3b</b>	12	14	17	19	23	24	20	23	18	18

<sup>a</sup> Values with uncertainties less than 5 %.

<sup>b</sup> Shannon, R. D.; Prewitt, C.T. *Acta Cryst.* **1969**, B25, 925; **1970**, B26, 1046; data quoted in Marcus, I. *Ion Properties*, Marcel Dekker: New York, 1997, pp 46-47.

**Table 2.** Logarithms of the stability constants ( $\log \beta \pm \sigma_{n-1}$ )<sup>a</sup> of lanthanide complexes with **1b**, **2b** and **3b** (Methanol,  $I = 0.01$  M in Et<sub>4</sub>NCl, Et<sub>4</sub>NNO<sub>3</sub> or Et<sub>4</sub>NClO<sub>4</sub>,  $T = 25$  °C)

Ligand	Method/medium	La <sup>3+</sup>	Pr <sup>3+</sup>	Eu <sup>3+</sup>	Gd <sup>3+</sup>	Yb <sup>3+</sup>
<b>1b</b>	Spec. / Cl <sup>−</sup>	$\geq 7$	$\geq 7$	$\geq 7$	$\geq 7$	$\geq 7$
	Spec. / NO <sub>3</sub> <sup>−</sup>	6.2±0.3	—	6.1±0.2	—	5.5±0.2
	Pot. / ClO <sub>4</sub> <sup>−</sup>	8.88±0.08	9.2±0.3	8.87±0.01	9.0±0.1	8.6±0.2
<b>2b</b>	Spec. / Cl <sup>−</sup>	5.5±0.2	4.9±0.1	4.7±0.4	4.3±0.3	3.4±0.1
	Spec. / NO <sub>3</sub> <sup>−</sup>	2.2±0.6	—	2.08±0.04	—	$\leq 2$
<b>3b</b>	Pot. / ClO <sub>4</sub> <sup>−</sup>	8.86±0.07	8.5±0.7	8.9±0.1	8.9±0.2	8.2±0.4

<sup>a</sup>Standard deviation  $\sigma_{n-1}$  on the mean of several experiments.

**Table 3.** Complexation thermodynamic parameters of lanthanide triflates with **1b**, **2b** and **3b** obtained by microcalorimetric titrations (Methanol,  $T = 25\text{ }^{\circ}\text{C}$ )

Ligand	Parameter	La <sup>3+</sup>	Pr <sup>3+</sup>	Eu <sup>3+</sup>	Gd <sup>3+</sup>
<b>1b</b>	$\log \beta$	8.88±0.08 (6.55) <sup>a</sup>	9.2±0.3	8.87±0.01	9.0±0.1
	$-\Delta G$ (kJ mol <sup>-1</sup> )	50.6±0.4 (37.34) <sup>a</sup>	52±2	50.56±0.06	51.3±0.6
	$-\Delta H$ (kJ mol <sup>-1</sup> )	26.34±0.07 (27.22) <sup>a</sup>	31.77±0.07	24.78±0.01	28±1
	$T\Delta S$ (kJ mol <sup>-1</sup> )	24.3±0.5 (10.12) <sup>a</sup>	21±2	25.78±0.07	23±2
<b>2b</b>	$\log \beta$	6.05±0.04 (3.0±0.04) <sup>a</sup>	6.31±0.05	6.0±0.1	5.43±0.03
	$-\Delta G$ (kJ mol <sup>-1</sup> )	34.5±0.2 (17.1±0.2) <sup>a</sup>	35.9±0.3	34.2±0.6	30.9±0.2
	$-\Delta H$ (kJ mol <sup>-1</sup> )	-38.9±0.4 (-17.7±0.5) <sup>a</sup>	-35±2	-38.5±0.4	-50.8±0.4
	$T\Delta S$ (kJ mol <sup>-1</sup> )	73.4±0.6 (34.8±0.7) <sup>a</sup>	71±2	73±1	81.7±0.6

<sup>a</sup>Titration with La(NO<sub>3</sub>)<sub>3</sub>

**Table 4.** Relevant proton chemical shifts ( $\delta$ , ppm) of ligands **1b**, **2b** and **3b** and its metal complexes

	<i>t</i> -Bu	ArCH <sub>2</sub> Ar		CH <sub>2</sub> OCH <sub>2</sub>		OCH <sub>2</sub> CO	ArH
		eq	ax	eq	ax		
<b>1b</b>	0.95, 1.17	3.27, 3.31	4.91, 5.08	4.67	4.89	4.36, 4.78, 4.90, 5.04	6.72, 6.90, 6.99, 7.02
<b>1b</b> + La <sup>3+</sup> (A)	1.18, 1.26	3.80, 3.83	4.26, 4.22	4.36	4.94	4.97, 5.04, 5.46, 5.49	7.20, 7.41, 7.45, 7.64
<b>1b</b> + La <sup>3+</sup> (B)	1.23, 1.26	<sup>a</sup>	<sup>a</sup>	4.33	4.90	<sup>a</sup>	7.17, 7.37, 7.41, 7.58
<b>2b</b>	1.08	—	—	4.62	4.94	4.57	6.98
<b>2b</b> + La <sup>3+</sup>	1.15	—	—	4.36	5.10	4.75	7.02
<b>3b</b>	1.07	3.19	5.29	—	—	5.02	6.78
<b>3b</b> + La <sup>3+</sup>	1.19	3.79	4.30	—	—	5.34	7.34

<sup>a</sup>Not possible to assign

**Figure 1.** Structural formulae of calixarenes.

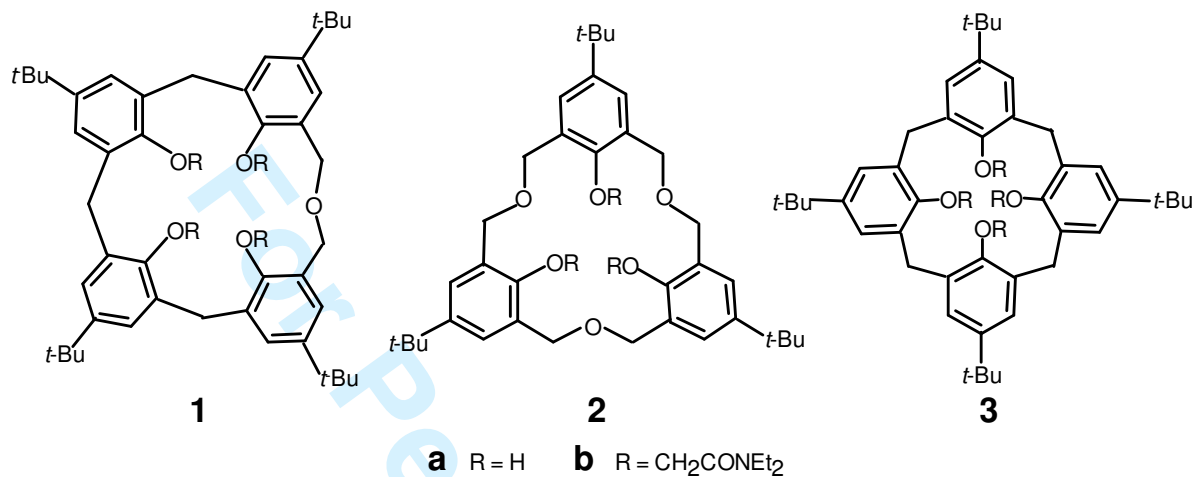
**Figure 2.** Spectrophotometric titration of **1b** ( $C_{1b} = 3.67 \times 10^{-4}$  M) with  $\text{PrCl}_3$  ( $0 \leq C_{\text{Pr}}/C_{1b} \leq 1.24$ ) in methanol at 25 °C.

**Figure 3.** Microcalorimetric titration of 2.5 mL of **1b** ( $4.43 \times 10^{-4}$  M) by addition of  $17 \times 15$   $\mu\text{L}$  of  $6.25 \times 10^{-3}$  M of  $\text{Gd}(\text{CF}_3\text{SO}_3)_3$  in methanol at 25 °C.

**Figure 4.** Microcalorimetric titration of 2.5 mL of **2b** ( $4.56 \times 10^{-4}$  M) by addition of  $17 \times 15$   $\mu\text{L}$  of  $6.25 \times 10^{-3}$  M of  $\text{Gd}(\text{CF}_3\text{SO}_3)_3$  in methanol at 25 °C.

**Figure 5.** Aromatic region of the  $^1\text{H}$  NMR spectra of **1b** in  $\text{CDCl}_3/\text{CD}_3\text{OD}$ , 22 °C and 500 MHz. (a) free ligand, (b) upon addition of 0.5, (c) 1 equiv and (d) 3 equivs. of  $\text{La}(\text{CF}_3\text{SO}_3)_3$ .

**Figure 6.** Job's plot based on  $^1\text{H}$  NMR data for the system **1b** +  $\text{La}^{3+}$ ; total concentration  $1 \times 10^{-2}$  M in  $\text{CDCl}_3\text{-CD}_3\text{OD}$  (9:1, v/v).



**Figure 1**

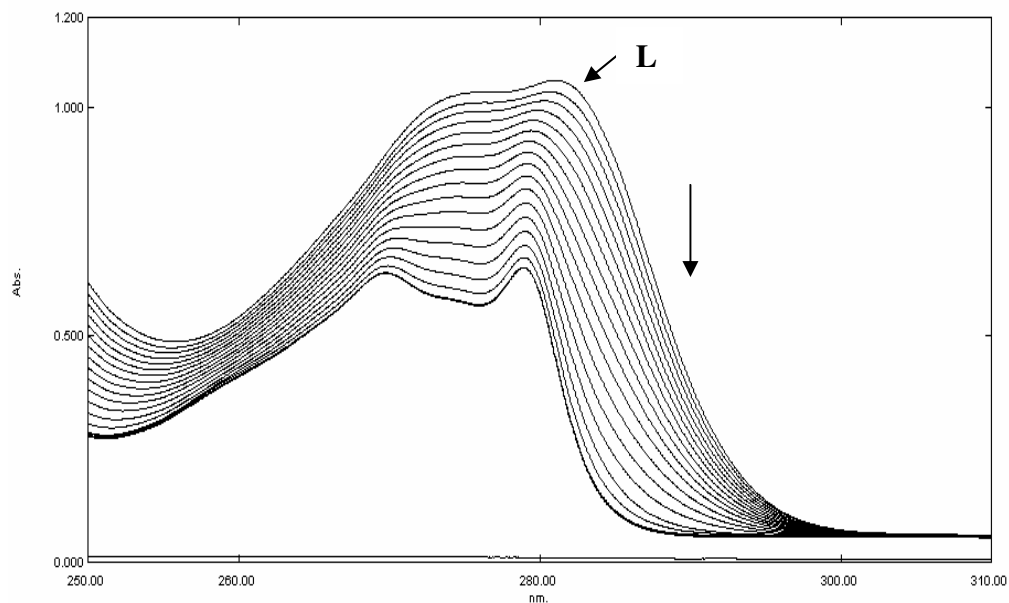
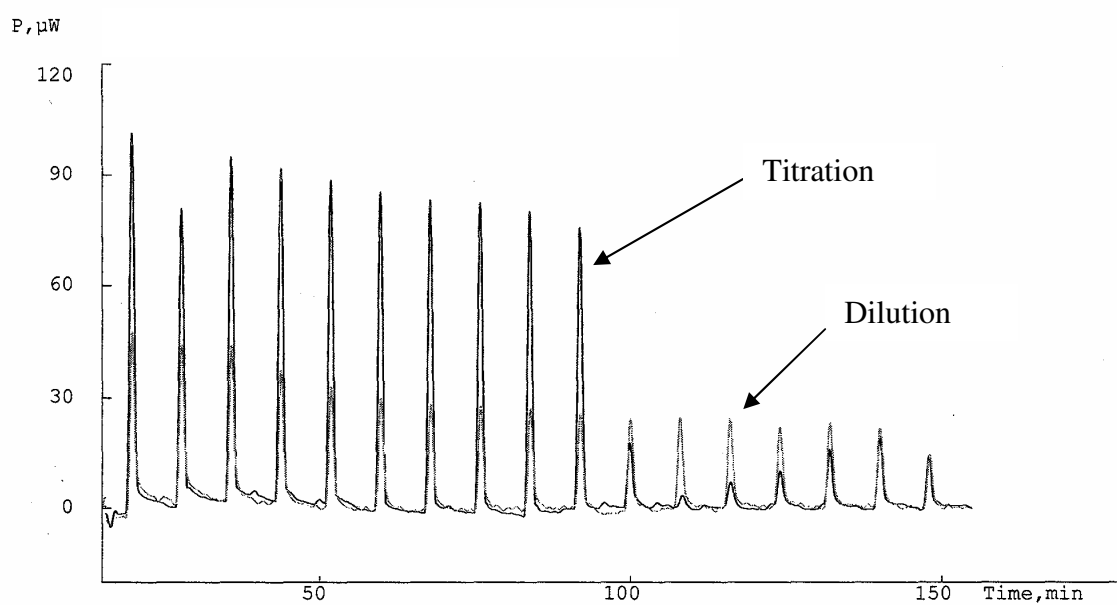


Figure 2

**Figure 3**



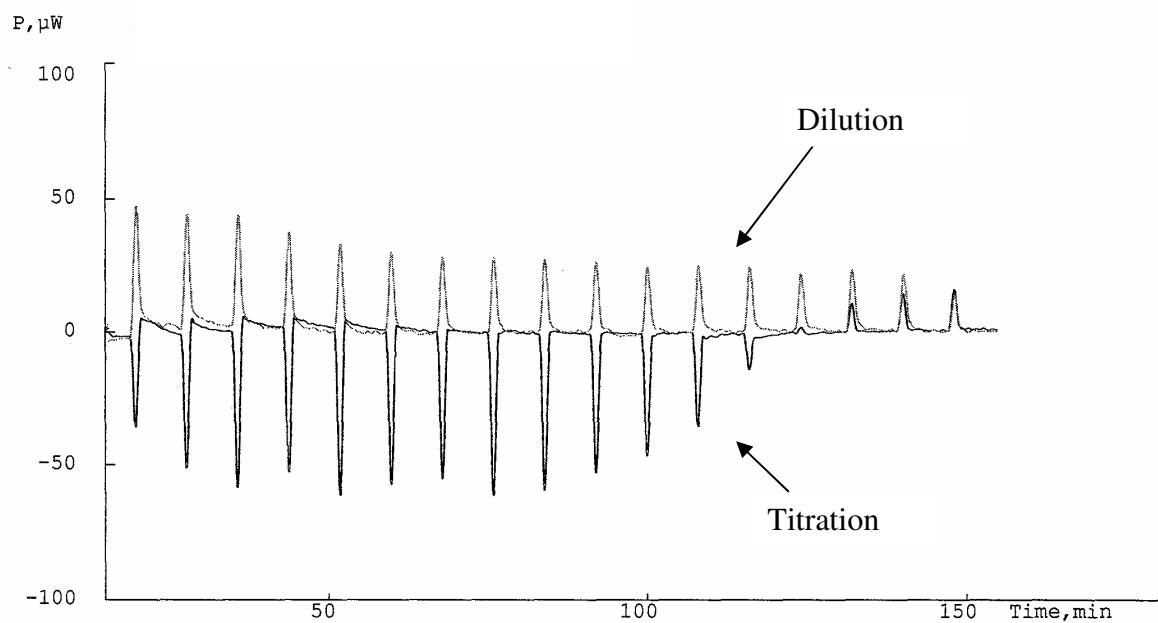
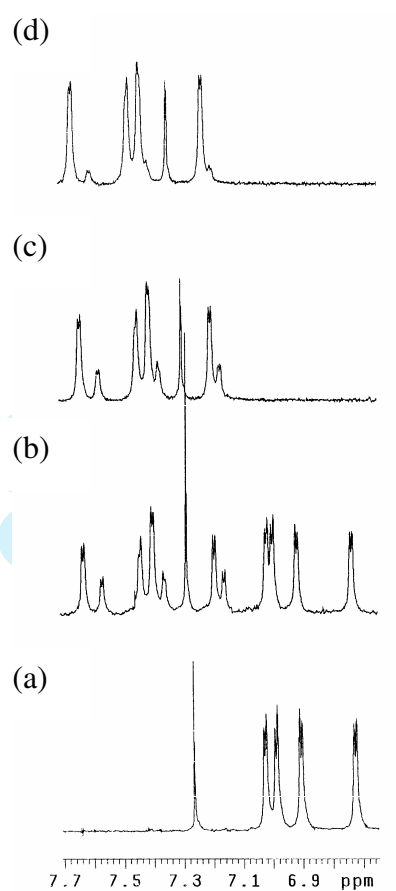


Figure 4

**Figure 5**

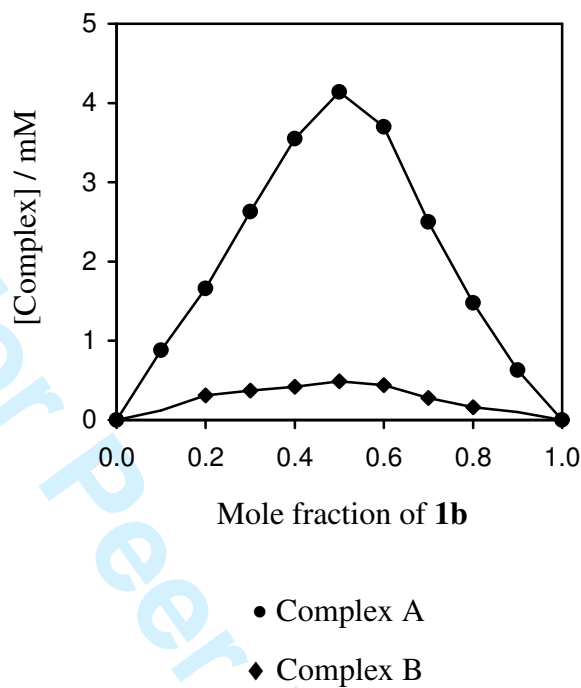
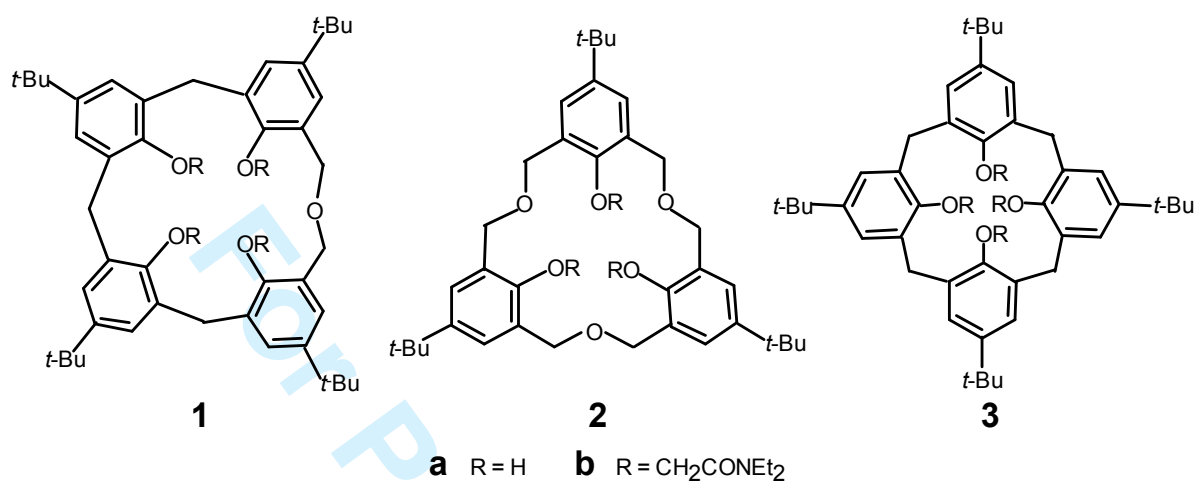


Figure 6



**Figure 1**

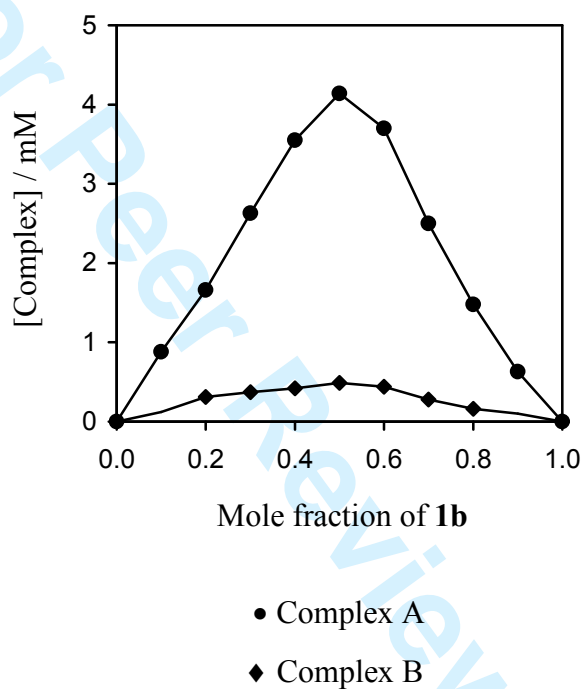


Figure 6