DALTON

Complexation of Pr^{3+}, Eu^{3+}, Yb^{3+} and Th^{4+} ions by calixarene carboxylates*

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The binding abilities of a series of ionizable calixarenes towards three lanthanides (Pr^{3+}, Eu^{3+} and Yb^{3+}) and one actinide (Th^{4+}) have been established in methanol by potentiometric measurements. The calixarenes result from progressive substitution of the phenolic hydrogens of *p-tert*-butylcalix[4]arene by carboxylic acid functions. Calixarene derivatives with mixed carboxylic and ester functional groups, as well as octa-*O*-carboxymethyl-*p-tert*-butylcalix[8]arene and the two oxa-derivatives, tetra-*O*-carboxymethyl-*p-tert*-butyltetrahomodioxacalix[4]arene and tri-*O*-carboxymethyl-*p-tert*-butylhexahomotrioxacalix[3]arene have also been studied. The formation of 1 : 1 species partially protonated $[M(H_zL)]$ and totally deprotonated (ML) as well as methoxo species $[\{ML(OMe)_z\}]$ has been established with lanthanides. Additional binuclear complexes and their methoxo forms have been found in some cases. With thorium the mononuclear ML and MHL complexes are mainly formed in addition to the corresponding methoxo species at high pH. For a given ligand, the stability of the complexes increases with the cationic charge: complexes of thorium are more stable than those of lanthanides, which are themselves generally more stable than the corresponding alkaline-earth- and alkali-metal complexes. The predominance of electrostatic interactions in the binding is further confirmed by a linear relationship between the stability of mononuclear complexes ($\log \beta_{110}$) and the total basicity of the ligands (ΣpK_{a_i}). The *p-tert*-butylcalix[8]arene octaacid and the *p-tert*-butylcalix[4]arene monoacid are respectively the best complexing agents for the lanthanides and thorium. The monoacid derivative shows significant Yb^{3+}/Eu^{3+} and Th^{4+}/Eu^{3+} selectivities in appropriate pH ranges.

As part of a study of the complexation properties of chemically modified calixarenes we reported earlier the acid–base characteristics of a series of calixarenes bearing ionizable carboxylic functions at the lower rim, and their complexing properties towards alkali- and alkaline-earth-metal cations.[2] The results of these studies showed that, under appropriate acidic conditions, calixarene carboxylic acids are very efficient complexing agents for these cations and are much stronger binders than calixarene esters, amides or ketones. We have extended our studies to include other significant cations and now report the complexing properties of these carboxylic derivatives towards three trivalent lanthanides (Pr^{3+}, Eu^{3+} and Yb^{3+}) as well as one tetravalent actinide (Th^{4+}). In addition to tetra-*O*-carboxymethyl-*p-tert*-butylcalix[4]arene **IVa**, we studied some derivatives with mixed functionalities such as O^1,O^3-bis(carboxymethyl)- **IIa**, O^1,O^3-bis(*tert*-butoxycarbonylmethyl)-O^2,O^4-bis(carboxymethyl)- **IIb**, *O*-carboxymethyl-**Ia**,O^1,O^2,O^3-tris(*tert*-butoxycarbonylmethyl)-O^4-carboxymethyl- **Ib**, O^1-carboxymethyl-O^2,O^3,O^4-tris(ethoxycarbonylmethyl)- **Ic** and O^1-carboxymethyl-O^3-ethoxycarbonylmethyl-*p-tert*-butylcalix[4]arene **Id**. Two oxa-derivatives, tetra-*O*-carboxymethyl-*p-tert*-butyltetrahomodioxacalix[4]arene **IVb** and tri-*O*-carboxymethylbutylhexahomotrioxacalix[3]arene **IIIc** have also been studied. Calix[8]arenes are represented in the series by octa-*O*-carboxymethyl-*p-tert*-butylcalix[8]arene **IVc**. The stability constants of the complexes have been determined in methanol. All calix[4]arenes are in the cone conformation, except for **IVb** which is in 1,2-alternate conformation.[2] The triacid **IIIc** is in the partial cone conformation and the octaacid **IVc** is conformationally mobile.

Experimental

Materials

The solvent, methanol (Carlo Erba with low water content, maximum 0.01% in weight), was used without further purification.

All the calixarenes were used as the free acids. Solutions were made by dissolution of a weighed quantity in MeOH in the presence of *ca.* 1 equivalent $HClO_4$. The ionic strength was held constant at 10^{-2} mol dm^{-3} by addition of tetraethylammonium perchlorate recrystallized twice from methanol. The titrant base used was tetraethylammonium hydroxide made from a dilution of the commercial solution (25% in MeOH, Fluka) and standardized against potassium hydrogen phthalate.

The metallic salts were the trifluoromethanesulfonates $M(O_3SCF_3)_3$ (M = Eu, Pr or Yb), synthesized according to a literature procedure.[3] The thorium salt was commercial $Th(NO_3)_4 \cdot 5H_2O$ (Merck, p.a.). The salts were dried at room temperature under vacuum before use. Their stock solutions were titrated by complexometry with ethylenedinitrilotetraacetate using xylenol orange as indicator.[4]

Preparation of calixarene acids

Tetraacid **IVa**,[5] monoacid triethyl ester **Ic**,[6] monoacid tri-*tert*-butyl ester **Ib**,[6] diacid **IIa**,[5] diacid di-*tert*-butyl ester **IIb**,[2] monoacid **Ia**,[2] dioxatetraacid **IVb**,[2] and monoacid monoester **Id**[7] were prepared according to the literature procedures.

Trioxatriacid IIIc. This compound was prepared from the known *p-tert*-butylhexahomotrioxacalix[3]arene **IIIa**[8] *via* triester **IIIb**. A mixture of **IIIa** (0.9 g, 1.2 mmol), ethyl bromo-

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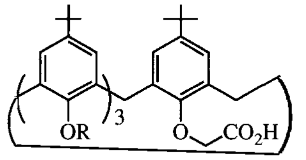
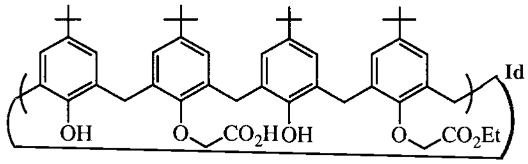
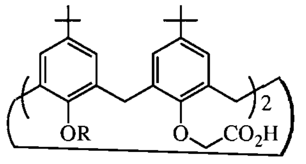
* Cation complexation by chemically modified calixarenes. Part 9.[1]



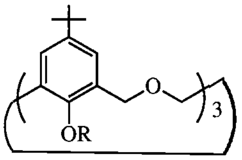
Ia R = H
Ib R = $CH_2CO_2Bu^t$
Ic R = CH_2CO_2Et



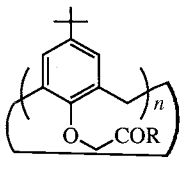
Id



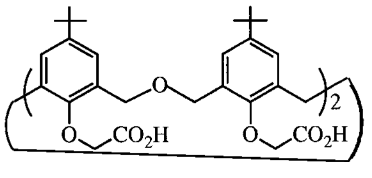
IIa R = H
IIb R = $CH_2CO_2Bu^t$



IIIa R = H
IIIb R = CH_2CO_2Et
IIIc R = CH_2CO_2H



IVa n = 4 , R = OH
IVc n = 8 , R = OH
IVd n = 8 , R = OEt
V n = 4 , R = NEt_2
VI n = 4 , R = NC_4H_8



IVb

acetate (1.2 g, 7.0 mmol) and anhydrous potassium carbonate (0.72 g, 5.2 mmol) in acetone (10 cm^3) was heated under reflux for 12 h. The cooled reaction mixture was filtered and the filtrate concentrated *in vacuo* to a yellow oil (1.23 g) which was chromatographed in dichloromethane over alumina to yield triester **IIIb** as a colourless solid, m.p. 152–153 °C. IR(KBr/cm^{-1}) 1750. ^{1}H NMR (C_6D_6, 400 MHz): δ 0.93 (3 H, t, CH_3), 1.02 (6 H, t, CH_3), 1.20 [18 H, s, $C(CH_3)_3$], 1.30 [9 H, s, $C(CH_3)_3$], 3.38 (2 H, s, OCH_2), 3.72 (2 H, q, $OC\mathit{H}_2CH_3$), 3.95 (4 H, q, $OC\mathit{H}_2CH_3$), 4.23 (2 H, d, OCH_2), 4.24 (2 H, d, arylCH_2O), 4.28 (2 H, d, arylCH_2O), 4.38 (2 H, d, arylCH_2O), 4.67 (2 H, d, OCH_2), 4.80 (2 H, d, arylCH_2O), 5.06 (2 H, d, arylCH_2O), 5.25 (2 H, d, arylCH_2O), 7.24 (2 H, d, aryl), 7.31 (2 H, d, aryl) and 7.45 (2 H, s, aryl).

Triester **IIIb** (1.0 g, 12 mmol) and potassium hydroxide (1.0 g, 17.8 mmol) were dissolved in ethanol (20 cm^3) and the mixture was heated under reflux for 90 min. The cooled mixture was concentrated to dryness and treated with 10% hydrochloric acid (2.0 cm^3) to form a precipitate which was filtered off, washed thoroughly with water and air dried to afford triacid **IIIc** (0.81 g, 90%), m.p. 136–138 °C. IR (KBr/cm^{-1}) 1750. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.29 [18 H, s, $C(CH_3)_3$], 1.33 [9 H, s, $C(CH_3)_3$], 2.58 (2 H, s, arylCH_2O), 3.91–5.19 (19 H, series of overlapping singlets and doublets, arylCH_2O, OCH_2, CO_2H), 7.30 (2 H, d, aryl), 7.38 (2 H, d, aryl) and 7.43 (2 H, s, aryl).

Octa-*O*-carboxymethyl-*p*-*tert*-butylcalix[8]arene IVc. The known octa-*O*-ethoxycarbonylmethyl-*p*-*tert*-butylcalix[8]arene **IVd**[9] (1.0 g, 0.5 mmol) in ethanol (40 cm^3) was treated with potassium hydroxide (1.0 g, 17.8 mmol) under reflux for 24 h. Work-up exactly as described above for triacid **IIIc** furnished octaacid **IVc** (0.34 g, 39%), mp 309–312 °C, after purification by crystallization from acetone–dimethyl sulfoxide. IR (KBr/cm^{-1}) 3600–2600, 1750. ^{1}H NMR [$(CD_3)SO$, 300 MHz]: δ 0.82–1.08 [72 H, br s, $C(CH_3)_3$], 3.31–3.48 (16 H, br s, arylCH_2), 3.88–4.00 (16 H, br s, OCH_2), 4.00–4.13 (8 H, br s, OH) and 6.84–6.93 (16 H, br s, aryl).

Stability constant determination

The stability constants of the complexes were determined potentiometrically using a competitive method with the proton. The concentrations of the free hydrogen ions, $[H^+]$, were measured with a combined glass electrode (Ingold) connected to an automatic titrator (Titro processor Metrohm 636), at 25 °C. The experimental procedure has been described in detail previously.[2] The pH notation used throughout the text stands for $-\log[H^+]$, since the standardization of the glass electrode has been made at $-\log[H^+] = 2$ with a solution of 10^{-2} mol dm^{-3} $HClO_4$ in methanol. As the junction potentials vary exponentially with $-\log[H^+]$,[10] the relationship (1) was used. Mean

$$-\log[H^+]_{real} = -\log[H^+]_{meas} + a + b[H^+]_{meas} \qquad (1)$$

values for a and b, determined by measuring the pH of a solution of 10^{-3} mol dm $^{-3}$ $HClO_4$ and 9 × 10^{-3} mol dm^{-3} NEt_4ClO_4 in methanol, were respectively +0.25 and −25. The experimental data were treated by the programs MINIQUAD[11] and SIRKO,[12] which refine the overall stability constant β_{xyz} of the complexes, corresponding to the equilibria (2). The protonation

$$xM^{m+} + yL^{n-} + zH^+ \rightleftharpoons M_xL_yH_z^{(xm-ny+z)+} \qquad (2)$$

constants β_{01z} of the deprotonated forms of the calixarenes were constant during the refinement procedure, as well as the formation constants β^*_{xz} of methoxo species, corresponding to the equilibria (3). The β_{01z} values were obtained by titration of

$$xM^{m+} + zMeOH \rightleftharpoons M_x(OMe)_z^{(xm-z)} + zH^+ \qquad (3)$$

the calixarenes in the absence of metal. Values for all except **IIIc** and **IVc** have been previously reported.[2,7] Those for **IIIc** and **IVc** have been determined in this work. For **IIIc**, log $\beta_{011} = 12.4$, log $\beta_{012} = 22.8$ and log $\beta_{013} = 31.5$. The octaacid **IVc** could be considered as a tetraacid H_4L since only four acidic functions could be neutralized. The corresponding constants are: log $\beta_{011} = 12.2$, log $\beta_{012} = 22.8$, log $\beta_{013} = 32.2$ and log $\beta_{014} = 40.2$. The β^*_{xz} values were determined by titrating solutions of lanthanide and thorium salts in methanol ($c_M \approx 10^{-3}$ mol dm^{-3}) with a maximum of 5 equivalents NEt_4OH. The autoprotolysis constant of methanol used for the calculations was $pK_{MeOH} = -16.7$.[13]

Results and Discussion

Methanolysis of the cations

The position of the inflection points on the titration curves of the three lanthanide salts in MeOH suggested the formation of the binuclear species $[Ln_2(OMe)_3]^{3+}$ and $[Ln_2(OMe)_5]^+$, in addition to the mononuclear species $[Ln(OMe)]^{2+}$, $[Ln(OMe)_2]^+$ and $Ln(OMe)_3$. In the case of thorium, the formation of $[Th(OMe)]^{3+}$, $[Th(OMe)_3]^+$, $Th(OMe)_4$ and $[Th_2(OMe)_7]^+$ was also revealed from the titration curves. The corresponding overall methanolysis constants β^*_{xz} are presented in Table 1. The additional species $[Yb_3(OMe)_5]^{4+}$ and $[Pr(OMe)_4]^-$ as well as $[Th_2(OMe)_5]^{3+}$ and $[Th_2(OMe)_9]^-$ were found to improve the fit significantly.

The distribution curves of the methoxo species as a function of pH established for $c_M = 10^{-3}$ mol dm^{-3} (Fig. 1) show that, as

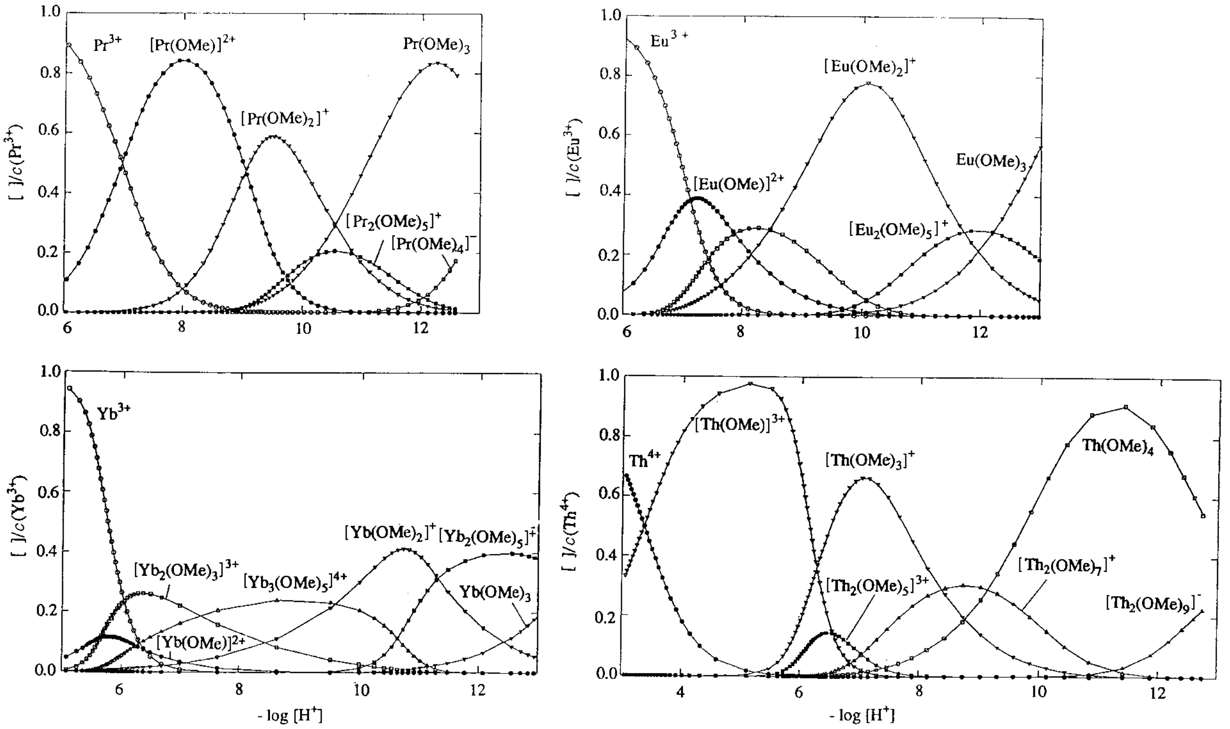


Fig. 1 Distribution curves of the mexthoxy species formed with Pr^{3+}, Eu^{3+}, Yb^{3+} and Th^{4+} *versus* $-\log[H^+]$ ($c_M = 10^{-3}$ mol dm^{-3})

Table 1 Values of $\beta_{xz} \pm \sigma_{N-1}$* for the methanolysis of Pr^{3+}, Eu^{3+} and Yb^{3+} (25 °C, I = 0.01 mol dm^{-3} NEt$_4$ClO$_4$)

$x:z$	Pr^{3+}	Eu^{3+}	Yb^{3+}	Th^{4+}
1 : 1	−6.96 ± 0.01	−7.11 ± 0.01	−6.40 ± 0.03	−3.36 ± 0.04
1 : 2	−16.01 ± 0.02	−15.27 ± 0.01	−13.48 ± 0.02	
1 : 3	−26.53 ± 0.01	−27.23 ± 0.02	−25.91 ± 0.04	−15.94 ± 0.05
1 : 4	−39.76 ± 0.04	—	—	−24.68 ± 0.04
2 : 3	—	−18.51 ± 0.03	−14.49 ± 0.03	
2 : 5	−39.05 ± 0.08	−38.66 ± 0.04	−34.75 ± 0.03	−22.6 ± 0.1
2 : 7	—	—	—	−36.6 ± 0.1
2 : 9	—	—	—	−59.2 ± 0.1
3 : 5	—	—	−23.53 ± 0.04	

* Arithmetic mean for N (⩾2) determinations.

expected from their respective charge densities, Yb^{3+} is more solvolysed than Pr^{3+}. At pH 6 there is only 30% free Yb^{3+} present instead of 90% Pr^{3+} and, at pH 7, no free Yb^{3+} left and still 50% Pr^{3+}. All methoxo species of Yb^{3+} coexist over the whole pH range, but none exceeds 40% formation, whereas [Pr(OMe)]$^{2+}$, Pr(OMe)$_3$, as well as [Eu(OMe)$_2$]$^+$ reach 80% formation.

Owing to the higher charge density, thorium (the 4+ species has a similar ionic radius as Eu^{3+}), is more solvolysed than the lanthanide cations. At pH 3.3 50% free thorium is left but 0% at pH 6. The species [Th(OMe)]$^{3+}$, [Th(OMe)$_3$]$^+$ and Th(OMe)$_4$ are predominant, respectively, below pH 6, between 6 and 8.5 and beyond 9. From pH 6 the formation of the condensed species [Th$_2$(OMe)$_5$]$^{3+}$, [Th$_2$(OMe)$_7$]$^+$ and [Th$_2$(OMe)$_9$]$^-$ range from 15 to 30% only.

Nature of the complexes

In all cases important pH lowerings were observed between the titration curves of the calixarenes alone and in the presence of the cations, suggesting the formation of very stable complexes. Again, the number and position of the equivalence points were indicative of the number and stoichiometry of the complexes formed, although in some cases the consideration of additional species led to significant improvement of the fit. Methoxo species were taken into account when pH lowering occurred after the expected final equivalence point. The species found for each ligand/cation system are given in Tables 2 and 3 together with the logarithms of the stability constants and their confidence intervals.

With the three lanthanide cations there is always formation of mononuclear ML$^{(3-n)+}$ complexes accompanied by some of their expected protonated M(H$_z$L)$^{(3-n+z)+}$ and methoxy ML(OMe)$_z^{(3-n-z)+}$ [or MLH$_{-z}^{(3-n-z)+}$] forms at lower and high pH, respectively. With diacid **IIb**, triacid **IIIc**, tetraacid **IVa**, and ligands **IVc** and **Ia**, behaving as tetraacids, the titration curves were compatible with the presence of binuclear M$_2$L$^{(6-n)+}$ complexes and, in most cases, some of their methoxo forms. Dimeric species have been found with **Ia**.

As regards thorium, there is always formation of mononuclear ThL$^{(4-n)+}$ species accompanied, for mono- and dicarboxylic calixarenes, by methoxy species only and in the other cases by methoxo and protonated species (mainly 1 : 1 : 1 species). In contrast to lanthanides, the presence of simple binuclear species was never established but in some cases the consideration of binuclear methoxo species as with **IIIc** and **Ia** significantly improved the fit.

Stability of the complexes

The lanthanide complexes are very stable, as shown by the high values of log β_{xyz}. In particular, the 1 : 1 : 0 complexes are more stable than the corresponding complexes of alkali- and alkaline-earth-metal cations.[2] For instance, europium(III) complexes with **Ia** and **Id** are respectively 11 and 14 log units more stable than the corresponding calcium complexes, and 14 and 19 logs units more stable than the corresponding sodium complexes. These results are explained by the higher charge of the lanthanide cations favouring electrostatic interactions with anionic ligands. However one exception should be noted: **IVa** forms an extremely stable calcium complex (log β_{110} = 22.4)[2] which is actually more stable than the corresponding lanthanide complexes. The high stability of the calcium complex had been explained by a positive co-operativity between charge and size effects. The fact that such an effect does not operate with lan-

Table 2 Values of log $\beta_{xyz} \pm \sigma_{N-1}$ * for the complexes formed with Yb^{3+}, Eu^{3+} and Pr^{3+} by calixarene carboxylic acids in MeOH (25 °C, $I = 0.01$ mol dm^{-3} NEt_4ClO_4)

Calixarene	$x : y : z$	Yb^{3+}	Eu^{3+}	Pr^{3+}
Ic (HL)	1 : 1 : 0	9.44 ± 0.01	8.37 ± 0.01	8.71 ± 0.01
	1 : 1 : −1	2.54 ± 0.03	0.00 ± 0.01	0.33 ± 0.02
	1 : 1 : −2	−4.94 ± 0.06	−8.3 ± 0.1	—
Ib (HL)	1 : 1 : 0	9.16 ± 0.04	8.37 ± 0.07	9.08 ± 0.01
	1 : 1 : −1	1.65 ± 0.01	0.00 ± 0.01	0.59 ± 0.01
	1 : 1 : −2	−9.03 ± 0.03	—	−10.9 ± 0.2
	2 : 2 : −3	−2.04 ± 0.05	—	−5.23 ± 0.05
IIa (H_2L)	1 : 1 : 0	15.7 ± 0.2	15.43 ± 0.06	14.91 ± 0.03
	1 : 1 : 1	18.4 ± 0.3	19.15 ± 0.07	18.67 ± 0.06
	1 : 1 : −1	11.0 ± 0.2	—	8.8 ± 0.2
IIb (H_2L)	1 : 1 : 0	14.49 ± 0.07	13.59 ± 0.03	13.56 ± 0.01
	1 : 1 : 1	20.90 ± 0.01	19.89 ± 0.03	20.37 ± 0.01
	1 : 1 : −1	—	3.27 ± 0.09	3.35 ± 0.06
	1 : 1 : −2	−5.86 ± 0.06	—	−7.89 ± 0.05
	2 : 1 : 0	—	18.30 ± 0.04	—
	2 : 1 : −1	13.5 ± 0.1	—	12.70 ± 0.02
	2 : 1 : −2	6.52 ± 0.06	—	4.09 ± 0.06
	2 : 1 : −3	−0.24 ± 0.08	−6.1 ± 0.1	−4.22 ± 0.03
	2 : 1 : −4	−12.13 ± 0.08	−18.3 ± 0.2	−16.7 ± 0.1
IIIc (H_3L)	1 : 1 : 0	21.3 ± 0.3	19.62 ± 0.02	20.54 ± 0.04
	1 : 1 : 1	28.3 ± 0.2	27.29 ± 0.02	27.51 ± 0.04
	1 : 1 : 2	—	31.91 ± 0.06	31.57 ± 0.07
	1 : 1 : −1	9.6 ± 0.3	7.18 ± 0.03	8.34 ± 0.09
	1 : 1 : −2	−2.3 ± 0.4	−4.9 ± 0.1	−3.37 ± 0.04
	2 : 1 : 0	26.4 ± 0.1	24.3 ± 0.4	25.50 ± 0.04
	2 : 1 : −1	20.3 ± 0.2	17.98 ± 0.03	17.83 ± 0.04
	2 : 1 : −3	1.7 ± 0.5	−2.7 ± 0.1	−2.10 ± 0.04
Id (H_3L)	1 : 1 : 0	25.2 ± 0.1	23.8 ± 0.1	23.53 ± 0.04
	1 : 1 : 1	30.5 ± 0.1	30.0 ± 0.1	29.3 ± 0.1
	1 : 1 : 2	34.2 ± 0.1	—	33.2 ± 0.1
IVa (H_4L)	1 : 1 : 0	20.5 ± 0.5	21.6 ± 0.1	17.9 ± 0.8
	1 : 1 : 1	32.8 ± 0.4	32.8 ± 0.1	30.7 ± 0.4
	1 : 1 : 2	38.45 ± 0.01	38.3 ± 0.1	38.1 ± 0.1
	2 : 1 : 0	31.3 ± 0.3	29.5 ± 0.5	30.64 ± 0.01
	2 : 1 : −2	12.8 ± 0.8	13.6 ± 0.2	9 ± 1
IVa (H_4L)	1 : 1 : 0	21.8 ± 0.2	21.1 ± 0.2	19.5 ± 0.5
	1 : 1 : 1	31.9 ± 0.2	31.4 ± 0.2	30.7 ± 0.5
	1 : 1 : 2	38.0 ± 0.2	37.8 ± 0.1	37.8 ± 0.5
	2 : 1 : 0	—	34.4 ± 0.4	—
	2 : 1 : −1	29.2 ± 0.3	29.3 ± 0.4	—
	2 : 1 : −3	5.5 ± 0.4	4.3 ± 0.4	
Ia (H_4L)	1 : 1 : 0	25.7 ± 0.1	18.96 ± 0.06	19.70 ± 0.06
	1 : 1 : 1	36.26 ± 0.01	31.10 ± 0.02	31.23 ± 0.05
	1 : 1 : 2	41.0 ± 0.1	—	—
	1 : 1 : 3	46.5 ± 0.1	—	45.77 ± 0.04
	1 : 1 : −1	12.6 ± 0.4	—	—
	2 : 1 : 0	—		31.5 ± 0.1
	2 : 1 : −1	—		20.6 ± 0.2
	2 : 2 : 1	—	54.88 ± 0.04	—
	2 : 2 : 3	—	76.24 ± 0.02	—
	2 : 2 : 4	—	83.30 ± 0.03	—
	2 : 2 : 6	—	95.47 ± 0.05	—
	2 : 2 : 7	—	100.46 ± 0.06	—

* Arithmetic mean of N (⩾2) determinations; negative z values refer to methoxo species.

Table 3 Values of log $\beta_{xyz} \pm \sigma_{N-1}$ * for the complexes formed with Th^{4+} by calixarene carboxylic acids in MeOH (25 °C, $I = 0.01$ mol dm^{-3} NEt_4ClO_4)

Calixarene	$x : y : z$	log β_{xyz}
Ic (HL)	1 : 1 : 0	9.9 ± 0.2
	1 : 1 : −1	5.25 ± 0.06
IIb (H_2L)	1 : 1 : 0	15.4 ± 0.1
	1 : 1 : −1	9.7 ± 0.2
	1 : 1 : −2	2.33 ± 0.01
	2 : 1 : −5	−8.19 ± 0.01
IIIc (H_3L)	1 : 1 : 0	23.09 ± 0.04
	1 : 1 : 1	28.6 ± 0.1
	1 : 1 : −1	15.1 ± 0.3
	2 : 1 : −2	20.68 ± 0.01
	2 : 1 : −4	7.91 ± 0.01
	2 : 1 : −5	−3.2 ± 0.1
	2 : 1 : −6	−15.8 ± 0.1
Id (H_3L)	1 : 1 : 0	26.73 ± 0.02
	1 : 1 : 1	31.70 ± 0.01
Ia (H_4L)	1 : 1 : 0	34.4 ± 0.1
	1 : 1 : 1	40.2 ± 0.1
	1 : 1 : 2	44.0 ± 0.3
	1 : 1 : −1	27.4 ± 0.1
	1 : 1 : −2	14.9 ± 0.1
IVa (H_4L)	1 : 1 : 0	29.53 ± 0.02
	1 : 1 : 1	34.61 ± 0.02
IVb (H_4L)	1 : 1 : 0	32.3 ± 0.3
	1 : 1 : 1	36.9 ± 0.1
IVc (H_4L)	1 : 1 : 0	27.9 ± 0.3
	1 : 1 : 1	34.2 ± 0.3
	2 : 1 : −3	22.9 ± 0.6

* Arithmetic mean for N (⩾2) determinations; negative z values refer to methoxo species.

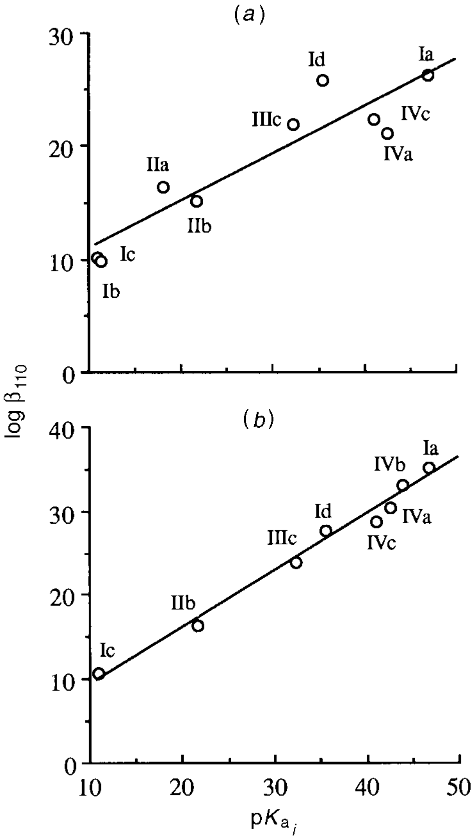


Fig. 2 Plot of log β_{110} *versus* ΣpK_{a_i} for the ligands studied: (*a*) Yb^{3+} and (*b*) Th^{4+}

thanides can be related to the strong solvation of these cations, which does not favour their introduction into the hydrophillic cavity of the ligand. On the contrary, the strong solvation of the cations could explain the formation of additional binuclear complexes in which the cations would be located outside the cavity of the ligand. Moreover, Yb^{3+}, possessing the higher charge density, is the most strongly bound among the three lanthanides.

The predominance of electrostatic interactions in the stability of these complexes is also demonstrated by the linear correlation between log β_{110} and ΣpK_{a_i}, the total basicity of the ligands. Fig. 2(*a*) illustrates the case of Yb^{3+}. The deviations observed with the tetraanionic ligand **IVa** or **IVc** could be explained by the formation of additional binuclear complexes. A similar increase in the complex stability with the total basicity of the ligands can be observed with the 2 : 1 : 0 complexes of Eu^{3+} and ligands **IIb**, **IIIc** and **IVa**. It should be noted, however, that the stability of the binuclear complex of Eu^{3+} with the octamer **IVc** is higher than expected from electrostatic

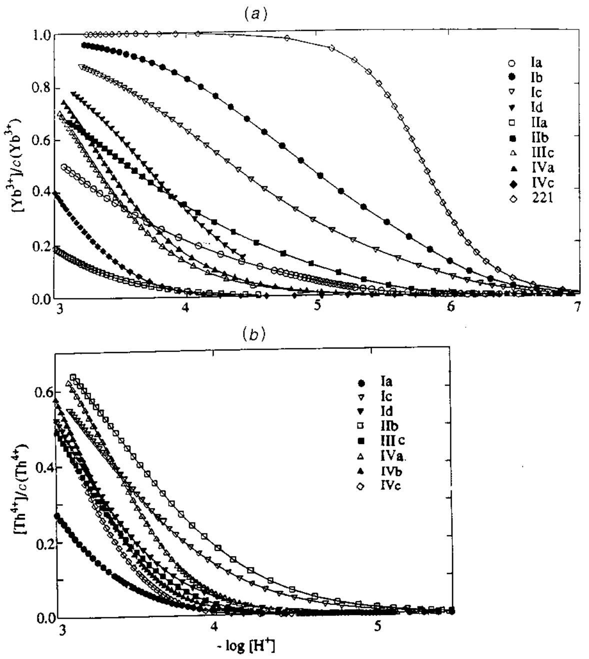


Fig. 3 Fraction of calculated free metal concentration *vs.* $-\log[H^+]$, for the ligands studied: (*a*) Yb^{3+} and (*b*) Th^{4+} ($c_M = c_L = 6 \times 10^{-4}$ mol dm^{-3})

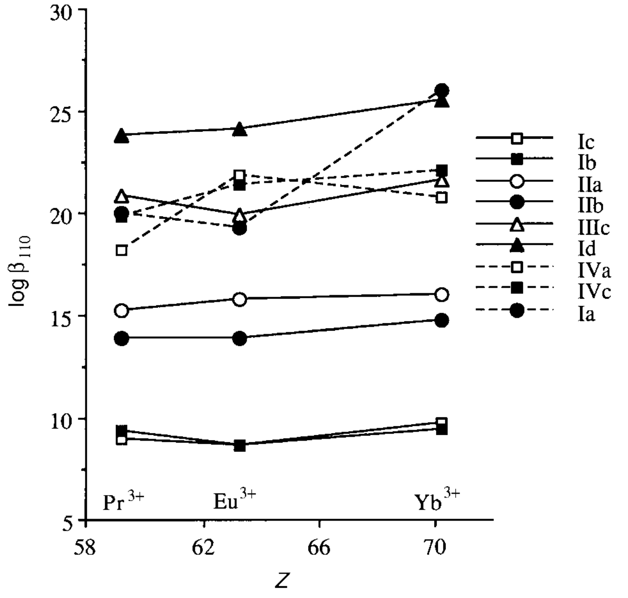


Fig. 4 Variation of $\log\beta_{110}$ *vs.* the atomic number of Yb^{3+}, Eu^{3+} and Pr^{3+}

considerations. In this case, the bigger hydrophilic cavity of the ligand could encapsulate two cations and efficiently bind them *via* four carboxylates and probably also the oxygen donor atoms of the other four unionized carboxylic groups. This illustrates a co-operative effect between the macrocyclic structure of the octamer and its anionic charges.

The plots in Fig. 3(*a*), giving the calculated fraction of free Yb^{3+} *versus* pH for the different ligands, provide another way of comparing their complexing power, independently of the type of complexes formed. The binding ability follows the sequence **Ib** < **Ic** < **IIb** < **Ia** < **Id** < **IVa** < **IIIc** < **IVc**. Even the simple monoacid **Ib** is a much stronger binder than cryptand 221 {4,7,13,16,21-pentaoxa-1,10-diazobicyclo[8.8.5]tricosane}.[14]

Only a qualitative comparison can be made with related macrocycles containing carboxylic functions, since all data available in the literature were obtained from aqueous solutions. Taking into account the decrease in stability of *ca.* 4.6 log units when moving from methanol to water (see protonation constants of acetate and phenoxyacetate in both media[2]), one can assume the 1:1:0 complexes of the diacids **IIa** and **IIb** to be as stable as the corresponding complexes of 1,10-diaza-4,7,13,16-tetraoxacyclooctadecane-*N*,*N*′-diacetate, for which $\log\beta_{110}(H_2O) = 10–12$.[15] In the same way, the stability of the complexes of tetraacid **IVa** should be comparable to that of their homologues of 1,4,8,11-tetraazacyclotetradecane-*N*,*N*′,*N*″,*N*‴-tetraacetic acid (H_4teta), for which $\log\beta_{110}(H_2O) = 14–16$,[16] but lower than that of the complexes of 1,4,7,10-tetraazacyclododecane-*N*,*N*′,*N*″,*N*‴-tetraacetic acid (H_4dota), for which $\log\beta_{110}(H_2O) = 28–29$.[16] On the other hand, the stability constants of the mononuclear complexes of the two calix[4]arene amines **V** and **VI** are of the same order of magnitude ($\log\beta_{ML} \approx 8$ in methanol)[17] as those of the monoacetates **Ib** and **Ic**, but much lower than those determined for the other carboxylate derivatives. However, it should be kept in mind that the complexing power of the neutral amide derivatives is high and pH independent which makes these ligands more efficient complexing agents than all the carboxylic derivatives in acidic media.

Table 4 Selectivities of complexation for the calixarenes studied: $S_1 = \beta_{110}(M^1)/\beta_{110}(M^2)$, $S_2 = \beta_{210}(M^1)/\beta_{210}(M^2)$

Calixarene	S_1(Yb/Eu)	S_2(Yb/Eu)	S_1(Th/Eu)	S_1(Th/Ca)	S_1(Th/Na)
Ic	11.8		31.6	1.1×10^4	1.6×10^4
Ib	6.2		—	—	—
IIa	1.9		—	—	—
IIb	7.9		63.1	—	6.3×10^8
IIIc	47.9	125.9	3.2×10^3	—	—
Id	25.1		7.9×10^2	7.9×10^{16}	2.0×10^{22}
IVa	0.07 *	63.0	7.9×10^7	1.3×10^7	4.0×10^{19}
IVb	—		—	—	3.2×10^{26}
IVc	5.1		6.3×10^6	—	2.0×10^{22}
Ia	5.5×10^6		2.5×10^{15}	3.2×10^{26}	1.6×10^{29}

* S_1(Eu/Yb) = 13.8.

The complexes formed with Th^{4+} and the acid derivatives are in all cases more stable than the complexes of lanthanides: stabilizations of respectively 3.5, 7.9 and 15.4 log units have been found with the triacid **IIIc**, the tetraacid **IVa** and the monoacid **Ia** with respect to Eu^{3+}. The stabilization of the thorium(IV) complex with **Ia** is huge when compared to the complexes of Ca^{2+} and Na^+: 26.5 and 29.2 log units, respectively. The higher stability of the complexes of thorium is again mainly due to the higher charge density of the cation. The stability of the 1:1:0 complexes of thorium linearly increases when going from monoacid **Ic** to diacid **IIb**, and then to trianionic ligands **IIIc** and **Id**, and tetraanionic ligands **IVa**, **IVb**, **Ia** and **IVc**, as clearly illustrated by the variation of $\log\beta_{110}(Th^{4+})$ with ΣpK_{a_i} [Fig. 2(*b*)]. This proportionality, which is even better than for lanthanides, again highlights the predominance of the electrostatic interactions in the complexation.

The global complexing ability of the ligands towards Th^{4+} is depicted in Fig. 3(*b*), showing the fraction of free Th^{4+} *versus* pH. The observed sequence is: **IIb** < **Ic** < **IVa** < **Id** < **IIIc** < **IVb** < **IVc** < **Ia**. Diacid di-*tert*-butyl ester **IIb** appears to be globally less efficient than monoacid triethyl ester **Ic**, probably due to the steric hindrance caused by the *tert*-butyl ester groups which disfavours the approach of the highly solvated Th^{4+} cation. Similarly, compounds **IVb**, **Ia**, **IIIc** and **IVc** present a sterically less hindered structure than **IVa**. In conclusion it appears that **Ic** and **IIb** are the least efficient complexing agents towards Th^{4+}, whereas all ligands bearing three or four anionic charges have comparable complexing abilities. However, the monoacid **Ia** is by far the best complexing agent for Th^{4+}. On the other hand, the stabilities of the 1:1:0 complexes of Th^{4+} and carboxylic calixarenes are quite comparable to those of their homologues with the very efficient acyclic aminopolycarboxylate *trans*-1,2-cyclohexalenedinitrilotetraacetate [log

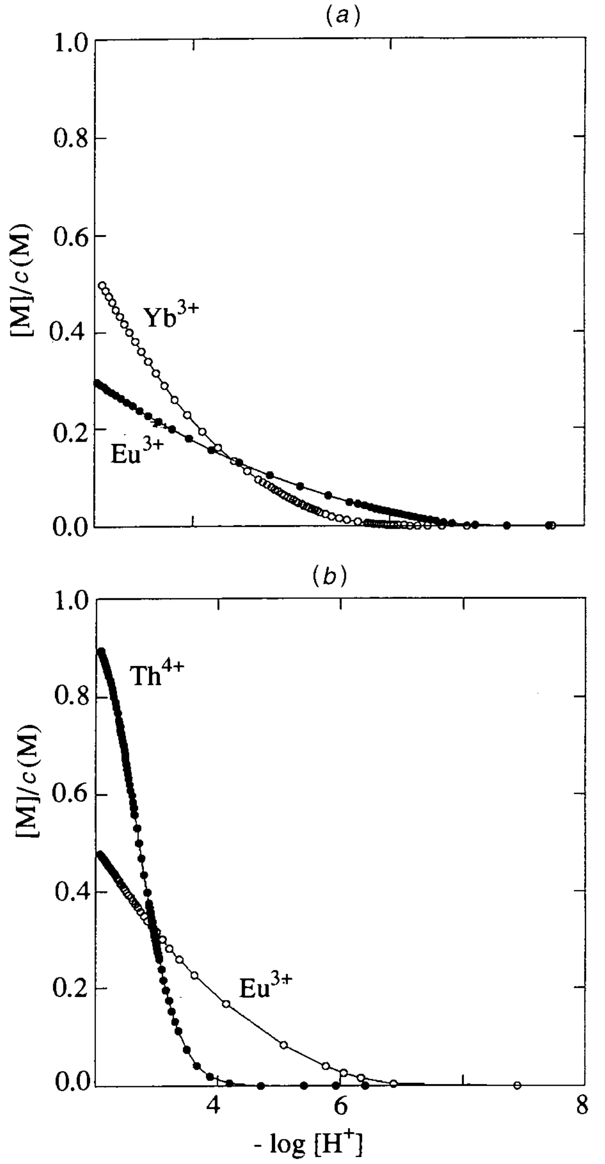


Fig. 5 Fraction of (*a*) free Yb^{3+} and Eu^{3+} and (*b*) free Eu^{3+} and Th^{4+} *vs.* $-\log[H^+]$ in the presence of compound **Ia** ($c_M = c_L = 6 \times 10^{-4}$ mol dm^{-3})

$\beta_{110}(H_2O) = 24.9$],[18] [(carboxymethyl)imino]bis(ethylenenitrilo)-tetraacetate [log $\beta_{110}(H_2O) > 27$],[18] and triethylenetetranitrilohexaacetate [log $\beta_{110}(H_2O) \gg 27$],[19] as well as with one efficient tetrahydroxamate ligand (log $\beta_{110} \approx 32$)[20] and the catecholate ligand *N*,*N*′,*N*″,*N*‴-tetrakis(2,3-dihydroxy-5-sulfobenzoyl)-1,5,10,14-tetraazatetradecane.[21]

Complexation selectivities

Fig. 4 represents the variation of log β_{110} *versus* the atomic number *Z* of the three lanthanide cations. Some selectivities for one cation (M^1) relative to another (M^2), expressed as the ratio of the stability constants $S_1(M^1/M^2) = \beta_{110}(M^1)/\beta_{110}(M^2)$ or $S_2(M^1/M^2) = \beta_{210}(M^1)/\beta_{210}(M^2)$, are given in Table 4.

With all calixarenes except **Ia** the variation of stability is not important. However, there is a small selectivity for Yb^{3+} over Eu^{3+}, S_1(Yb/Eu) ranging from 1.9 to 48. An exceptionally high S_1(Yb/Eu) of 5.5 × 10^6 is found for the monoacid **Ia**. This result however should be modulated, since only mononuclear species are found with Yb^{3+}, whereas also dimeric complexes are formed with Eu^{3+}. A more adequate way of interpreting the real selectivity of **Ia** is provided by the comparison of the calculated fraction of free Yb^{3+} and Eu^{3+} left in solution, *versus* pH, independently of the type of complexes formed. Fig. 5(*a*) represents the calculated fraction of each cation considered separately ($c_{Yb} = c_{Eu} = c_L = 6 \times 10^{4+}$ mol dm^3) in the presence of **Ia**. In fact, **Ia** is selective for Yb^{3+} only in the range $4.3 \leqslant pH \leqslant 6.5$. Before pH 4.3, **Ia** appears to be globally selective for Eu^{3+} since there is more complexed Eu^{3+} than Yb^{3+}. Considering an equimolar mixture of both cations in the presence of the free ligand ($c_L = c_{Yb} = c_{Eu} = 12 \times 10^{-4}$ mol dm^{-3}) does not change the selectivity pattern significantly. This implies the potential use of **Ia** under appropriate pH conditions for the separation of these cations.

All the calixarenes are selective for Th^{4+} relative to Na$^+$, Ca$^+$ or Eu^{3+}, the best being again the monoacid **Ia**, with S_1(Th/Eu) = 2.5 × 10^{15}, S_1(Th/Ca) = 3.1 × 10^{26} and S_1(Th/Na) = 1.6 × 10^{29}. The high selectivities relative to Na$^+$ and Ca^{2+} are obviously due to the fact that **Ia** does not bind these cations efficiently.

Simulation of the fraction of free Eu^{3+} and Th^{4+} for the systems **Ia**–Th and **Ia**–Eu [Fig. 5(*b*] shows that **Ia** is selective for Th^{4+} in the range $3 \leqslant pH \leqslant 6.5$. This observation again implies the potential use of **Ia** for the separation of trivalent actinides, modelled by Eu^{3+}, and tetravalent actinides, modelled by Th^{4+}. This is of particular interest since these cations are present in radioactive waste.

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