ORIGINAL ARTICLE

Novel phosphorylated calixarenes for the recognition of *f*-elements

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Abstract The binding properties of three series of phosphorylated calixarene derivatives bearing phosphine oxide or phosphonate groups either at the wide or the narrow rims have been investigated towards some representative lanthanide and actinide ions using several approaches: (i) liquid–liquid extraction of europium, americium, thorium and uranyl ions from nitric acid solutions into the two diluents *m*-nitrobenzotrifluoride (*m*-NBTF) or dichloromethane; (ii) complexation in single media (methanol and acetonitrile) followed by UV-spectrophotometric and isoperibolic (micro)calorimetric titrations (ITC). The latter technique was found to be very useful for the determination of the stoichiometries of the complexes formed, in particular when the complexation did not induce significant spectral changes. It also provided a full thermodynamic characterization of these new systems. The influence of some structural features of the ligands as the nature of the substituents and the condensation degree of the calixarene moiety, on the distribution coefficients and on the complexation thermodynamic parameters has been established.

Introduction

Efficient reprocessing of high level nuclear wastes (HLW) arising from the generation of nuclear energy remains one of the most crucial problems nowadays [1]. Long lived radionuclides, especially actinides, are the most hazardous components of these wastes. The recovery of these elements from the total waste mass, alone or combined with other elements like lanthanides and technetium, before disposal or reprocessing (transmutation), should significantly enhance the ecological safety and the efficiency of the nuclear fuel cycle. A number of selective extracting agents have already been tested to recover these radionuclides, like monodentate organophosphorus extractants (e. g. trioctyl phosphine oxide (TOPO)) [2]. However, they possess low efficiency and insufficient selectivity affording no separation of hazardous radionuclides from acidic HLW. Therefore, efforts have been made to find new efficient extractants. One option was to attach donor phosphoryl groups to rigid platforms like calixarenes to take advantage of the proximity of these groups and thus create a synergistic effect enhancing the efficiency and the selectivity [3–5]. Tetramer derivatives bearing carbamoylmethylphosphine oxides (CMPO) at different positions of the calixarenic moiety have been extensively studied as well as some calixarenes substituted with phosphine oxides at the narrow rim [6, 7]. In the continuity of these works we report now on

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the binding properties of novel phosphine oxide and phosphonate derivatives of calix[n]arenes (Chart 1) with some representative lanthanides and actinides. This study is focusing on (i) the liquid–liquid extraction, from nitric acid into m-nitrobenzotrifluoride (m-NBTF) or dichloromethane of some lanthanides and actinides by these ligands and (ii) the thermodynamic characterization of europium(III) and uranyl(VI) complexes in methanol and acetonitrile using UV absorption spectrophotometry and Isoperibolic Titration Calorimetry (ITC). Comparison between extraction and complexation results is made, in particular in terms of the stoichiometries of the complexes formed. Correlations are also attempted between these data and some structural features of these ligands like the nature of the functional groups, the nature of the substituents and the condensation degree.

Results and discussion

Wide rim phosphine oxide derivatives

Liquid–liquid extraction experiments from nitric acid of various concentrations (0.1–6 M) into m-NBTF were first performed as screening tests to evaluate the binding properties of these compounds toward Eu^{3+}, Am^{3+} and UO_2^{2+} metal ions (Supplementary materials, Table S1). The extraction of the three cations followed the same trends but different behaviors were observed according to the ligand. When significant extraction levels were observed (i.e. for all ligands except **1a**, **1d** and **3b**), a more or less pronounced maximum of the D values is observed for nitric acid concentrations between 0.1 and 1 M. For example, for compounds **1**, this maximum is shifted towards the highest nitric acid concentrations when the substituent R_2 becomes small (Fig. 1). This particular behavior was explained by the remarkable solubility of these ligands (especially **1b** substituted by the small ethyl substituents) in low concentrated nitric acid which was confirmed by the determination of their partition coefficients [8]. For ligands **1c** and **1e** substituted with the longer propyl and butyl residues this trend appears simply as a decrease of D with the increasing nitric acid concentration which can be ascribed to the competitive extraction of the proton.

The synergistic or "co-operative" effect due to a synergism or a "co-operation" induced by the proximity of the binding arms organized on the calixarene scaffold can be measured from the comparison of the extraction results with those obtained with simple phosphine oxides like TOPO or the monomeric subunit **0c**. This effect, evaluated by the ratio of the distribution coefficients obtained with both ligands, was found to be 400 for the maximum extraction of europium by ligand **1e** (at 0.1 M nitric acid), as compared to its monomeric subunit **0e**.
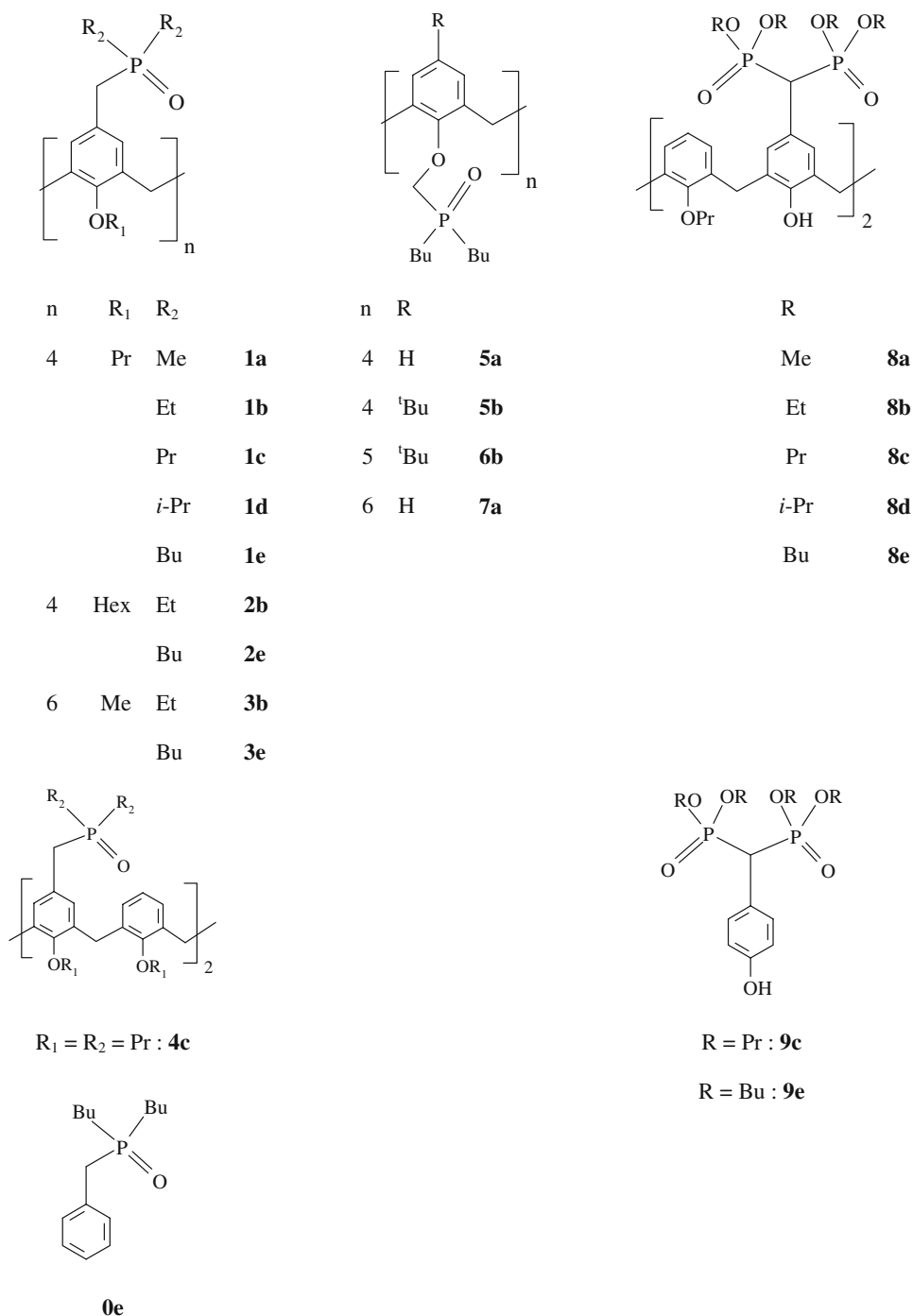
The influence of several structural parameters like the condensation degree or the number of functional groups, and the length of the alkyl radicals R_1 and R_2 could be discussed [7, 9]. It was found that tetramers are better extractants than hexamers and that, contrary to that of R_2, the nature of R_1 has only very little influence of the extraction properties of these ligands.

The analysis of the slopes of the linear plots log D versus the logarithm of the concentration of the ligand in the organic phase allowed the determination of the complex stoichiometry (Table 1). Europium and americium are extracted as disolvates (1:2 complexes) by the tetramers **1**, as well as by the hexamer **3e**, certainly accompanied with a monosolvate (1:1 complex) with the latter ligand and europium. In contrast uranyl seems to be always extracted as a 1:1 complex with most of these ligands.

Extraction of europium and thorium nitrates was also performed from 1 M nitric acid into dichloromethane (Fig. 2). It can be seen that the percentage of europium extracted decreases regularly with the size of the substituent, contrary to the situation in m-NBTF where **1b** (R_2 = Et) is the best extractant from 1 M nitric acid. For thorium the sequence of extraction is different, showing an unexpected increase of extraction with **1e**. These results allow comparison with previous data obtained with other phosphorylated calix[4]arenes and show that these ligands are less efficient than most of the related wide rim CMPO calix[4]arenes [5, 10].

Although extraction methods are widely used to assess the binding ability of a ligand, its affinity for a given cation is more clearly described by the stability constant of the complex formed in a single solvent which does not depend on the lipophilicity of the system. Therefore complexation was followed in two different solvents: methanol whose properties are close to those of water and acetonitrile in which the interactions are expected to be stronger. UV absorption spectrophotometric titrations were first performed in both solvents but the spectral changes induced by the complexation were very weak (Electronic materials, Fig. S1). Different models were used to interpret the experimental data but in many cases all of them were able to reproduce the experimental data with more or less the same accuracy. In these conditions it was difficult to select the best one. However, some trends could be observed as the formation of 1:1 complexes with some representative lanthanides (La^{3+}, Eu^{3+} and Yb^{3+}) and ligands **1d,e** and **3e** in both media and 2:1 complexes with uranyl in methanol with **1d,e**.

Since the spectrophotometric results lack reliability, microcalorimetry (or ITC) was used to investigate the binding abilities of these ligands. This technique presents the advantage to provide with a full thermodynamic characterization of the systems studied, i. e. the stability

Chart 1 The phosphorylated calixarenes studied

n	R₁	R₂	
4	Pr	Me	**1a**
		Et	**1b**
		Pr	**1c**
		i-Pr	**1d**
		Bu	**1e**
4	Hex	Et	**2b**
		Bu	**2e**
6	Me	Et	**3b**
		Bu	**3e**

n	R	
4	H	**5a**
4	ᵗBu	**5b**
5	ᵗBu	**6b**
6	H	**7a**

R	
Me	**8a**
Et	**8b**
Pr	**8c**
i-Pr	**8d**
Bu	**8e**

R₁ = R₂ = Pr : **4c**

R = Pr : **9c**

R = Bu : **9e**

0e

constants and the complexation enthalpy (ΔH) and entropy ($T\Delta S$) contributions. We focused our investigations on europium and uranyl ions with **1c** and **1e** in methanol and with **1c**, **1e** and **1d** in acetonitrile.

In methanol, the signals corresponding to the titration of both cations are exothermic. Examples of thermograms are given in the electronic material (Fig. S2 and S3). After correction of the dilution effects, they were slightly endothermic for europium and **1e** and still exothermic in the

other cases. They were all interpreted by the formation of 1:1 species (Table 2). But for europium and **1e**, the fits were improved if an additional 2:1 species was considered. The stability constants found for the europium 1:1 complexes are of the same order of magnitude as those determined from spectrophotometric titrations (e.g. 4.4 and 4.3, respectively, with **1e**).

In acetonitrile, the thermograms are quite different. With europium and ligands **1c,d** they present highly
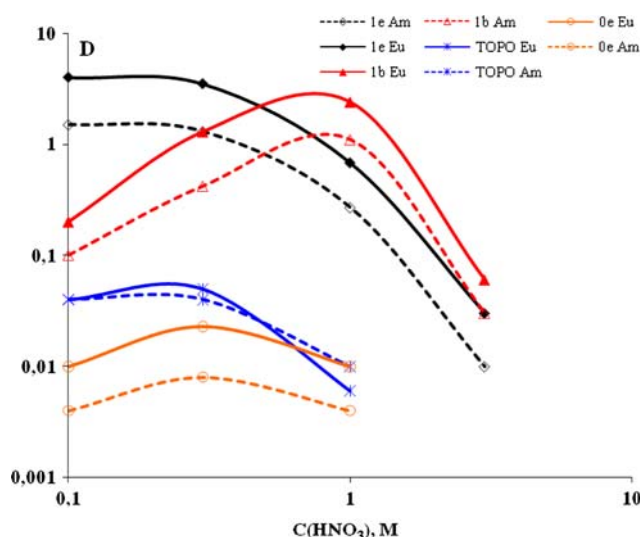
Fig. 1 Distribution coefficients D of ^{241}Am and ^{152}Eu from nitric acid solutions into m-NBTF containing the wide rim phosphine oxide calixarenes **1b** and **1e** (0.01 M), the monomer **0e** (0.04 M) and **TOPO** (0.04 M)

Table 1 Slopes of the variations log D vs. log (concentration of ligand) with the wide rim phosphine oxide calixarenes. (0.3 M HNO$_3$, into m-NBTF, unless otherwise stated)

Ligands	Eu^{3+}	Am^{3+}	UO$_2^{2+}$
1b[a]	1.7	1.7	1.2
1c[b]	1.7	1.8	1.0
1e	1.7	1.8	1.3
2b	–	–	1.4
2e	0.9	0.9	1.2
3e	1.5	1.8	0.9

[a] At 1 M HNO$_3$ into dichloroethane

[b] At 1 M HNO$_3$

exothermic peaks, then becoming endothermic and reaching at the end of the titration the values corresponding to the dilution, thus suggesting the formation of two complexes (Supplementary materials, Fig. S4). This was indeed corroborated by the interpretation which showed the presence of a 1:1 complex accompanied with a 2:1 species at higher metal concentrations. However, reverse titrations performed by adding the ligand **1c** into the metal solution, indicated unambiguously the formation of only the 1:1 species. Direct titration of **1e** showed the formation of the 1:1 species only. With uranyl ion highly exothermic peaks are observed (Supplementary materials, Fig. S5). Titrations of **1c** were also performed using the reverse procedure and the results obtained from both types of experiments show the formation of a 1:1 complex with log $\beta = 4.20$ (direct procedure) or 4.92 (reverse titration). Ligands **1d** and **1e**

with bulkier substituents form 1:1 and 2:1 complexes with very similar thermodynamic parameters. In all cases the stability of the complexes is higher in acetonitrile than in methanol.

The calorimetric results show that the main complexes which form in both solvents with the cations studied are 1:1 complexes sometimes accompanied with 2:1 species. In these neutral single media there is no evidence for the formation of 1:2 species with europium as in extraction from nitric acid solutions. It can be seen that in methanol, for the europium complexes the entropy term ($T\Delta S$) is largely dominant over the enthalpy contribution ($-\Delta H$), whereas the reverse situation is observed in acetonitrile. Desolvation effects prior to complexation may account for this difference as acetonitrile is less solvating than methanol. The stabilization of the uranyl complexes, in contrast, is always from enthalpic origin, the entropy contribution being strongly negative (unfavourable) especially in acetonitrile.

The comparison of the results obtained in acetonitrile shows that the nature of the substituent does not lead to large differences in the thermodynamic parameters of complexation. The stability of the 1:1 complex of europium seems, however, to decrease with the length of the substituent R_2 from Pr to Bu. The same trend is observed with uranyl but in this case the maximum of stability is observed when $R_2 = i$-Pr (**1d**), which corresponds to the least unfavourable entropy term.
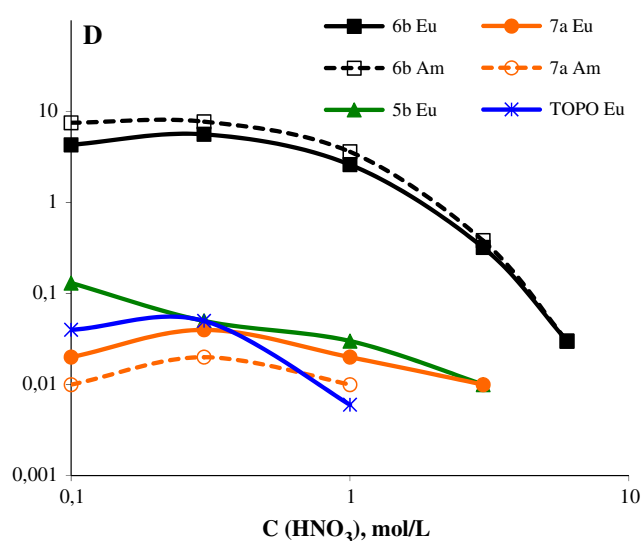
Narrow rim phosphine oxide derivatives

Four calix[n]arene derivatives of different degrees of condensation ($n = 4$, 5 and 6), all substituted with di-butyl phosphine oxide groups at the narrow rim were studied (Chart 1). Two of them are devoid of *tert*-butyl groups at the *para* position (R = H), the other bearing this substituent on this position. Liquid–liquid extraction experiments of Eu^{3+}, Am^{3+} and UO$_2^{2+}$ metal cations were carried out from nitric acid solutions into m-NBTF with these derivatives. The distribution coefficients D (Supplementary materials, Table S2) obtained were shown to depend on the acidity of the aqueous phase. The shape of the curves $D = f(C_{HNO_3})$ differs with the cation and to a lesser extent with the ligand, as shown in Fig. 3 for europium and americium and in Fig. 4 for uranyl. The D values of Am^{3+} and Eu^{3+} present a maximum for a HNO$_3$ concentration close to 0.3 M with all ligands except **5b**. Those of uranyl decrease when the nitric acid concentration increases with all ligands except **6b** which shows a maximum for a HNO$_3$ concentration near 1 M. This behavior is consistent with a competition between the extraction of the metal ions and of the proton, as seen classically with **TOPO** and phosphorylated extractants in general.
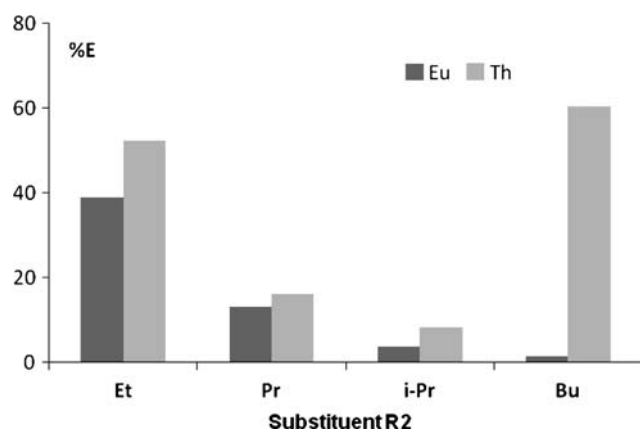
Fig. 2 Extraction of europium and thorium nitrates (10^{-4} M) by wide rim phosphine oxide calix[4]arenes from 1 M nitric acid into dichloromethane : influence of the length of the alkyl substituent R_2 on the percentage extraction Ligand concentration: 10^{-3} M for thorium; 10^{-2} M for europium

Fig. 3 Distribution coefficients D of ^{241}Am and ^{152}Eu from nitric acid solutions into m-NBTF containing the narrow rim phosphine oxide calix[n]arenes **5b**, **6b** and **7a** (0.01 M) and **TOPO** (0.04 M)

The extractability of all the narrow rim substituted calixarenes studied depends strongly on the condensation degree and hence on the number of functional groups attached to the ligand and on its size and conformation. As regard europium and americium extraction, the *p-tert*-butylcalix[5]arene **6b** possesses much greater extraction efficiency than its tetrameric counterpart **5b**. It is also more efficient than the hexamer **7a** but the fact that this

compound is *p*-dealkylated may also decrease its extractability as observed with the tetramers **5a** and **5b**. At 1 M nitric acid, the extractability for uranyl increases with the condensation degree or with the number of binding sites, according to the sequence:

Table 2 Stability constants (log β)[a] and thermodynamic parameters[a] (kJ mol^{-1}) of europium and uranyl complexes with wide rim phosphine oxide calixarenes in methanol and acetonitrile, at 25 °C, obtained by microcalorimetry and in brackets by spectrophotometry

Cations	Ligands	Complexes	log β	$-\Delta G$	$-\Delta H$	$T\Delta S$
Methanol						
Eu^{3+}	**1c**	**1:1**	4.93 ± 0.01(3.9)	28.10 ± 0.06	4 ± 1	24 ± 1
	1e	**1:1**	4.3 ± 0.3(4.4)	25 ± 2	−0.5 ± 0.2	25 ± 2
		2:1	6.8 ± 0.5	39 ± 3	−13 ± 2	52 ± 5
UO$_2^{2+}$	**1c**	**1:1**	2.85 ± 0.07	16.3 ± 0.4	40 ± 1	−24 ± 1
	1e	**1:1**	3.56 ± 0.04	20.3 ± 0.2	31 ± 2	−11 ± 2
Acetonitrile						
Eu^{3+}	**1c**	**1:1**	5.7 ± 0.3	33 ± 2	106 ± 2	−73 ± 4
		2:1	8.8 ± 0.5	50 ± 3	91 ± 2	−41 ± 5
		1:1[b]	5.79 ± 0.04	33.0 ± 0.2	106 ± 3	−73 ± 3
	1d	**1:1**	5.8 ± 0.2	33 ± 1	95 ± 10	−62 ± 11
		2:1	9.7 ± 0.5	55 ± 3	117 ± 8	−62 ± 11
	1e	**1:1**	5.2 ± 0.1	29.6 ± 0.6	102 ± 4	−72 ± 5
UO$_2^{2+}$	**1c**	**1:1**	4.20 ± 0.06	23.9 ± 0.3	96 ± 6	−72 ± 6
		1:1[b]	4.92 ± 0.04	28.0 ± 0.2	89 ± 9	−61 ± 9
	1d	**1:1**	6.2 ± 0.5	35 ± 3	85.7 ± 0.7	−50 ± 4
		2:1	10.6 ± 0.6	60 ± 6	125 ± 7	−65 ± 13
	1e	**1:1**	5.9 ± 0.3	34 ± 2	97 ± 3	−63 ± 5
		2:1	10.6 ± 0.6	60 ± 3	105 ± 4	−45 ± 7

[a] Mean value of at least three independent experiments; confidence interval: $\pm\sigma_{n-1}$, the standard deviation on this mean

[b] Reverse titration
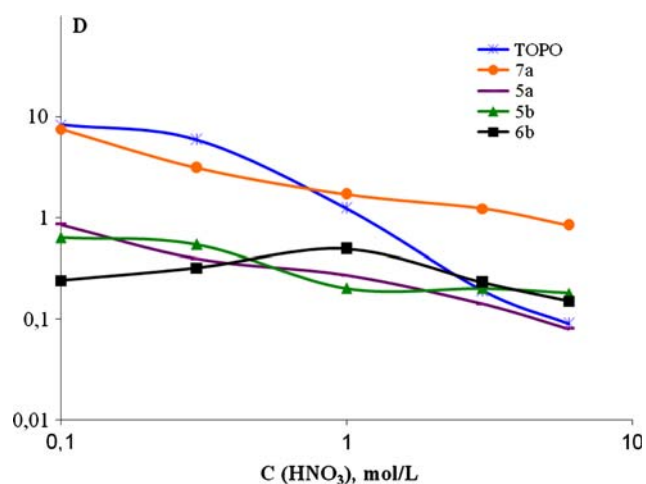
Fig. 4 Distribution coefficients *D* of uranyl from various nitric acid solutions into *m*-NBTF containing narrow rim phosphine oxide calix[*n*]arenes (0.001 M) and **TOPO** (0.004 M)

5b < 5a < 6b < 7a

Compound **7a** with six phosphoryl donor groups in a rather flexible arrangement is the best extractant for uranyl. This is consistent with X-ray crystallographic studies which have established that UO_2^{2+} complexes adopt either a pseudoplanar penta- or hexacoordinate structure which is quite different from the coordination structure of the other metal ions [11, 12].

It is worth noting that only the pentamer **6b** extracts europium and americium much better than **TOPO**. The other derivatives have more or less similar performances, depending on the acidity of the aqueous phase. In the case of uranyl nitrate extraction, the values of the distribution coefficients are even smaller than those of **TOPO** and the calixarene scaffold does not promote the extraction efficiency.

The stoichiometry of the extracted complexes into *m*-NBTF with the narrow rim substituted calixarenes could be determined by the slopes of the linear plots log *D* = *f* (ligand concentration) [8] which are summarized in Table 3. The pentamer **6b** extracts europium and americium as monosolvates, whereas the tetramer **5a** (R = H) likely extracts the two cations as a mixture of mono- and

Table 3 Slopes of the variations log *D* vs. log (concentration of ligand) with the narrow rim phosphine oxide calixarenes. (0.3 M HNO_3, into *m*-NBTF)

| Ligands	Eu^{3+}	Am^{3+}	UO_2^{2+}
5a	1.4	1.5	1.7
5b	–	–	1.1
6b	1.1	1.1	1.8
7a	–	–	1.4

disolvates. For uranyl extraction, the stoichiometry of the extracted complex depends on the ligand: 1:1 with the *p-tert*-butyl tetramer **5b** and 1:2 for the dealkylated **5a** and for the pentamer **6b**. With the hexamer **7a**, the results are consistent with a mixture of two complexes in solution: a predominant monosolvate (1:1 complex) accompanied by a disolvate (1:2 complex).

Some extraction experiments were performed using dichloromethane as diluent (Fig. 5). The percentage extraction, %E, of europium and thorium nitrates vary with the condensation degree and the *para*-substituent R. As in extraction into *m*-NBTF, the pentamer **6b** is a very good extractant for europium which is also well extracted by the *p*-dealkylated tetramer **5a**. **6b** is the best extractant of thorium cation. It is interesting to note that all these ligands are less efficient extractants than the lower rim CMPO *p-tert*-butylcalix[4]arene [13].

As with the wide rim derivatives, spectrophotometric titrations did not lead to reliable results, due to the weak spectral changes induced by the complexation. However, with lanthanides in methanol different models were tested and could be easily distinguished except with Eu^{3+} and **5b**. The best models imply the formation of 1:1 complexes. In the other cases it was impossible to select the best models since all of them fit the experimental data as satisfactorily. Nevertheless, a 2:1 species was found with uranyl ion and **5b**. Therefore microcalorimetric titrations were performed in methanol and acetonitrile in the case of europium and uranyl ions. The results are summarized in Table 4.

With the tetramers **5a,b** the signals were very weak. In the beginning of the titration of **5b** they were exothermic; after a metal to ligand concentration ratio of about 0.5 they became slightly endothermic and eventually exothermic again as the dilution (Supplementary materials, Fig. S6). This case was interpreted by the formation of 1:1 and 1:2
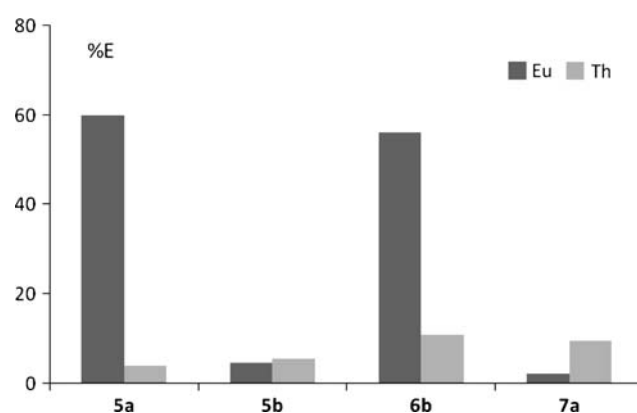
Fig. 5 Extraction of europium and thorium nitrates (10^{-4} M) by narrow rim phosphine oxide calix[4]arenes from 1 M nitric acid into dichloromethane Ligand concentration : 10^{-3} M for thorium; 10^{-2} M for europium

Table 4 Stability constants (log β)[a] and thermodynamic parameters[a] (kJ mol^{-1}) of europium and uranyl complexes with **5a**, **5b**, **6b** and **7a** in methanol and acetonitrile, at 25 °C, obtained by microcalorimetry and in brackets by spectrophotometry

Cations	Ligands	Complexes	log β	$-\Delta G$	$-\Delta H$	$T\Delta S$
Methanol						
Eu^{3+}	**5a**	**1:1**	4.5 ± 0.2(3.8)	26 ± 1	−15 ± 2	41 ± 3
	5b	**1:1**	4.55 ± 0.03(3.9)	25.9 ± 0.2	−10.7 ± 0.3	36.6 ± 0.5
		1:2	7.72 ± 0.06	44.0 ± 0.3	1.6 ± 0.1	42.4 ± 0.4
	6b	**1:1**	4.8 ± 0.9	27 ± 5	5 ± 1	22 ± 6
	7a	**1:1**	2.9 ± 0.2	17 ± 1	−6 ± 1	23 ± 2
UO$_2^{2+}$	**5a**	**1:1**	4.7 ± 0.1	26.8 ± 0.6	12 ± 2	15 ± 3
	5b	**1:1**	5.1 ± 0.4	29 ± 2	16.7 ± 0.3	12 ± 2
	6b	**1:1**	2.7 ± 0.1	15.4 ± 0.6	34 ± 3	−19 ± 4
	7a	**1:1**	3.26 ± 0.03	19 ± 2	32 ± 1	−13 ± 3
Acetonitrile						
Eu^{3+}	**5a**	**1:1**	4.14 ± 0.05	23.6 ± 0.2	76 ± 5	−52 ± 5
	6b	**1:1**	7 ± 1	40 ± 6	82 ± 1	−42 ± 7
		2:1	11 ± 2	68 ± 12	111.2 ± 0.5	−48 ± 14
UO$_2^{2+}$	**5a**	**2:1**	10.7 ± 0.1	61.0 ± 0.6	92 ± 1	−31 ± 2
	6b	**1:1**	3.72 ± 0.08	21.2 ± 0.4	135 ± 7	−114 ± 7
	7a	**1:1**	3.6 ± 0.2	21 ± 1	155 ± 18	−134 ± 19

[a] Mean value of at least three independent experiments. Confidence interval: $\pm\sigma_{n-1}$, the standard deviation on this mean

species. The comparison between the experimental corrected heat effect (Q_c) *vs.* the volume of titrant (metal ion solution) and the calculated heat effect assuming (a) a 1:1 species and (b) the two 1:1 and 1:2 species showed that the goodness of the fit is much higher when considering the two complexes (Supplementary materials, Fig. S7). The stability of the 1:1 complex found by this technique is higher than that derived from spectrophotometric titrations (Table 4).

As regard the pentamer **6b** and the hexamer **7a**, their interaction with europium produces exothermic effects. These effects are not very strong, especially when corrected for the dilution, but enough to propose a 1:1 stoichiometry for the species formed. The stability constant of the europium complex with the pentamer **6b** is, within the experimental error, of the same order of magnitude as those found with the tetramers (log β = 4.8 and 4.5, respectively), whereas much smaller (log β = 2.9) with the hexamer **7a**. In contrast, the heat effects produced by uranyl complexation are strongly exothermic and in all cases could be interpreted unambiguously by the formation of 1:1 complexes.

In acetonitrile, microcalorimetric titrations performed with **5a**, **6b** and **7a** are strongly exothermic (Supplementary materials, Fig. S8). With europium, the tetramer **5a** (R = H) and the pentamer **6b** (R = *tert*-Bu) form a 1:1 species, accompanied with a 2:1 complex in the case of **6b**. With the hexamer **7a**, the complexation of europium gives rise to very complicated thermograms showing two strong

exothermic heat effects followed by an endothermic step increasing at the end until it reached values corresponding to the dilution effect. This shape obviously shows the existence of at least two phenomena corresponding to the formation of a very stable 2:1 complex but the thermograms could not be interpreted. This could be due to the nature of **7a**, which is a *p*-dealkylated hexamer, much more flexible than the lower oligomers. With uranyl, the thermograms could be interpreted by the formation of 1:1 complexes with **6b** and **7a**, and of a 2:1 species with **5a**.

The calorimetric results showed that the stabilization of the europium 1:1 complexes in methanol is generally of entropic origin ($T\Delta S > 0$) with negative $-\Delta H$ values, except with **6b** for which it is slightly positive. The absence or presence of *p-tert*-butyl group on the tetramer (compare **5a** with **5b**) has no great influence on the thermodynamic parameters, but there is a compensation effect between the enthalpy term ($-\Delta H$), which increases from the tetramers to the pentamer **6b**, with the entropy term ($T\Delta S$) which decreases. In acetonitrile the stabilization is purely enthalpy driven, these terms being much more important than in methanol as expected in a less solvating solvent.

As regards uranyl ion in methanol, the higher stability of its 1:1 complexes with the tetramers is due to favourable enthalpy and entropy contributions. With the pentamer and the hexamer there are a strong increase of $-\Delta H$ and a decrease of $T\Delta S$ becoming negative. This shows that the enhanced bonding due certainly to the greater number of binding sites is counterbalanced by conformational

reorganization. In acetonitrile the situation is again characterized by very high enthalpy ($-\Delta H$) and very negative entropy ($T\Delta S$) values.

Wide rim phosphonate derivatives

Liquid–liquid extraction experiments of Eu^{3+} and Am^{3+} cations were carried out in the same conditions as with the phosphine oxide derivatives. The values of the distribution coefficients (Supplementary material, Table S3) with **8c** (R = Pr), which are very high as compared to the other calixarenes, decrease regularly when the nitric acid concentration increases and both cations are extracted with the same efficiency (Fig. 6). In contrast, the distribution coefficients with the related linear phosphonate **9c** (R = Pr) increase slightly with the acidity of the medium, and they are about 10^6 times lower than those observed with **8c**. This enormous difference in the extraction ability seems to be a specific behaviour of **8c**, since no "cooperative effect" higher than 10 was observed for the other calixarene phosphonates (compare **8e** and **9e**, for example). **8d** and **8e** extract americium ion more efficiently than europium ion.

No direct correlation was found between the extractability of these compounds and the size of the alkyl substituents R. **8c** (R = Pr) is the most effective compound, whereas **8e** (R = Bu) is the less effective one. The other derivatives present similar extraction abilities.

The apparent solvate numbers in *m*-NBTF were determined for **8b** (R = Et) and **8c** (R = Pr). There are practically no significant variations in the stoichiometry

Fig. 6 Distribution coefficients D of ^{241}Am and ^{152}Eu from nitric acid solutions into *m*-NBTF containing wide rim substituted phosphonate calix[4]arenes (0.01 M) solutions and related phosphonate subunits
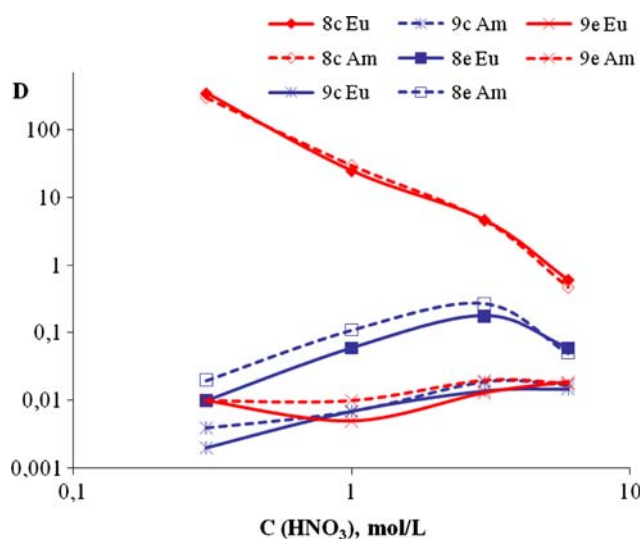
complexes with **8b**. Similar values were found for the slopes of the linear plots log D versus log (ligand concentration) for the extraction of europium and americium ions, 1.7 and 1.6, respectively. They suggest the simultaneous formation of two 1:1 and 1:2 complexes. On the contrary, quite different values of the slopes were found with **8c**. The value of 1.3 estimated for europium suggests the formation of a ML complex, whereas the value of 2.6 found with americium is more consistent with a ML_2 complex. This difference in the stoichiometry of the extracted complex may be advantageous for further americium and europium separation.

Extraction experiments of europium and thorium nitrates from 1 M HNO_3 into dichloromethane performed with **8c** and **8e** confirmed the better efficiency of the former ligand: %E values of 60 and 24 were found for europium and thorium ions, respectively, with the propyl derivative **8c**, instead of 5 and 7 with the butyl derivative **8e**.

UV-spectrophotometric titrations were performed in methanol with calixarene phosphonates, and with these systems also very weak spectral variations were observed. In these conditions, the interpretations were quite difficult. With **8c** and europium ion, the formation of M_2L (log β = 6.7) led to the best interpretations, whereas with **8e** only a 1:1 complex (log β = 3.9) was found. For uranyl ion complexation with both ligands, the interpretation was consistent with the formation of a 2:1 complex, slightly more stable with **8c** (log β = 7.53) than with **8e** (log β = 6.60). Changing the solvent from methanol to acetonitrile did not enhance the spectral variations upon complexation.

In order to estimate the stoichiometry and the stability constants of the species, microcalorimetric titrations were performed in methanol and acetonitrile. With this method, regarded as much more accurate than spectrophotometry in this case, we hoped in particular to confirm the behaviour of compound **8c** shown in extraction. Some representative thermograms corresponding to the titration of europium and uranyl nitrates with **8c** and **8e** in methanol and acetonitrile are shown in the supplementary material (Fig. S9–S12).

In methanol the thermal effects produced by the titration of the ligands with both cations were found to be exothermic and rather weak. After correction for the dilution (also exothermic) they were very small and therefore the interpretation of the data, i. e. the selection of the best model, was not obvious. The results are summarized in Table 5. With europium ion and **8c**, they showed the formation of a single complex ML_2 associated with a small positive enthalpy change. With **8e** the best model corresponded to a 1:1 species (log β = 3.3) but the value of the complexation enthalpy was determined with a poor accuracy, being very close to zero. This stoichiometry and the

Table 5 Stability constants (log β)[a] and thermodynamic parameters[a] (kJ mol^{-1}) of europium and uranyl complexes with **8c** and **8e** in methanol and acetonitrile, at 25 °C, obtained by microcalorimetry and in brackets by spectrophotometry

Cations	Ligands	Complexes	log β	$-\Delta G$	$-\Delta H$	$T\Delta S$
Methanol						
Eu^{3+}	**8c**	**1:2**	6.2 ± 0.1	35.3 ± 0.6	−6 ± 1	41 ± 2
	8e	**1:1**	3.30 ± 0.05(3.9)	18.8 ± 0.3	−3 ± 2	22 ± 2
UO$_2^{2+}$	**8c**	**1:2**	6.0 ± 0.2	34 ± 1	18.8 ± 0.7	15 ± 2
	8e	**1:2**	5.77 ± 0.01	32.90 ± 0.06	19 ± 4	14 ± 4
Acetonitrile						
Eu^{3+}	**8c**	**1:1**	5.46 ± 0.06	31.1 ± 0.3	55.0 ± 0.3	−24 ± 1
	8e	**1:1**	6.5 ± 0.1	37.0 ± 0.6	58 ± 3	−21 ± 4
UO$_2^{2+}$	**8c**	**2:1**	10.0 ± 0.2	57 ± 1	50 ± 3	7 ± 4
	8e	**2:1**	11.7 ± 0.7	67 ± 4	56 ± 1	11 ± 5

[a] Mean value of at least three independent experiments. Confidence interval: $\pm\sigma_{n-1}$, the standard deviation on this mean

stability constant value are consistent with the spectrophotometric result (log β = 3.9). It should be recalled that the log-log plot analysis suggested that europium was extracted from 0.3 mol/L nitric acid into *m*-NBTF as 1:1 and/or 1:2 complexes with ligands **8b** and **8c**. With uranyl ion, the effects, after correction of the dilution, are more important and still exothermic. They can be interpreted with both ligands by the presence of a 1:2 complex with small negative (exothermic) enthalpy changes.

In acetonitrile, the thermograms corresponding to the complexation of europium with ligands **8c** and **8e** are more complicated than in methanol. The signals are highly exothermic until a metal to ligand ratio of *c.a.* 1. Then, they become strongly endothermic, with values more positive than those corresponding to the dilution, before reaching at the end values close to the dilution. With both ligands the first part of the thermograms has been well interpreted by the presence of a 1:1 complex (Table 5). But obviously a second phenomenon is taking place afterwards, which could correspond to the formation of 2:1. However, taking into account such a species was not always satisfactory. With uranyl ion, the thermograms present exothermic peaks until a metal to ligand concentration ratio of *c.a.* 2, followed by endothermic signals corresponding to the dilution. An acceptable fit was obtained considering one M$_2$L species.

The results obtained with phosphonates show the formation of a great variety of complexes depending on the metal, the solvent and the ligand. For instance europium **8c** forms a 1:2 complex in methanol and a 1:1 complex in acetonitrile, while the dominant extracted species into *m*-NBTF seems to be a 1:1 complex. Concerning the stabilization of the 1:1 complexes the same trends as for phosphine oxide derivatives are found, i. e. the entropic contribution becomes unfavourable in acetonitrile as a consequence of the lower solvation in the latter solvent.

The stabilization of the 1:2 complexes of uranyl with both ligands in methanol is similar originating from favourable enthalpy and entropy terms, whereas for the 1:2 complex of europium with **8c** it is only due to the entropy which overcomes an unfavourable enthalpy term.

Conclusion

In conclusion, liquid–liquid extraction and complexation experiments have demonstrated the high affinity of new phosphine oxide and phosphonate calixarene derivatives towards europium, americium and uranyl cations. In the absence of significant spectral changes upon complexation by these ligands, calorimetric titrations have been very useful to show the formation of different kinds of complexes and to determine their thermodynamic parameters ΔG, ΔH and $T\Delta S$. Wide rim and narrow rim phosphine oxide derivatives form generally 1:1 complexes with europium and uranyl accompanied in some case with 2:1 complexes. These stoichiometries are not necessarily in agreement with those of the extracted complexes. It has been shown that the nature of the substituents does not lead to strong variations of the thermodynamic parameters, in contrast to the condensation degree which induces more changes. With the phosphonate derivatives different stoichiometries were shown according to the cation, the solvent and the substituent on the ligand. However, the complexation data found for the propyl derivative do not explain the particularly high extractability of this compound for europium as compared to the other derivatives. The origin of the stabilization of the complexes is quite different for the two cations and depends on the solvent. Whereas the entropy terms are generally favorable in methanol for europium complexes, the entropy contributions appear to be very negative and hence unfavourable in

acetonitrile. This points out the importance of the solvation/desolvation in the complexation processes. In contrast, the stabilization of the uranyl complexes is mostly enthalpy driven in both solvents.

Experimental

Materials

The phosphorylated calixarenes under study were synthesized at the Institute of Organic Chemistry of the National Academy of Sciences of Ukraine, Kiev, Ukraine according to the already published procedures [14–18]. They have all been characterized by the classical analytical methods and are all in the cone conformation (verified by ^{1}H NMR spectroscopy) except the hexamers which are stereochemically flexible in solution due to the free rotation of the arene subunits through the large macrocyclic annulus. The diluents, *m*-nitrobenzotrifluoride (*m*-NBTF from Rhodia) and dichloromethane CH_2Cl_2, and the solvents, methanol (Carlo Erba, 99.9%) and acetonitrile (Riedel-deHaën, analytical reagent), were used without further purification. The metal salts used were lanthanide, thorium and uranyl nitrates. They were dried under vacuum for at least 24 h before use and the concentrations of their stock solutions were standardized by complexometry using xylenol orange as coloured indicators [19]. Tetraethylammonium nitrate (Et_4NNO_3, Acros) used as supporting-electrolyte in the spectrophotometric titrations was dried under vacuum at room temperature.

Liquid–liquid extraction into *m*-NBTF

The distribution coefficients of Am and Eu were determined radiometrically from the γ-radiation of the corresponding isotopes. The experimental protocol is fully detailed in [8] and [9]. The distribution ratios of uranium were obtained according to the following procedure: the extractant solutions in *m*-NBTF were contacted with nitric acid solutions of different concentrations (from 0.1 to 6 M), containing 10^{-5} M [233]U. Extraction was performed in plastic tubes. The contact time was 3 min and the temperature was set at (23 ± 2) °C. Then the organic and the aqueous phases were separated and samples ($V = 0.2$ mL) were placed on special steel targets to be burned out and measured under vacuum. The activities of the targets were determined radiometrically by alpha-radiation of the [233]U isotope. The measurement error did not exceed 15%. The distribution coefficients were then calculated from the expression $D = A_{org}/A_{aq}$, where A is the specific activity of the radionuclide in the organic and the aqueous phases.

Liquid–liquid extraction into dichloromethane

The percentage extraction of europium and thorium nitrates ($C_M = 10^{-4}$ M) from a 1 M HNO_3 solution into a dichloromethane solution containing the ligand ($C_L = 10^{-2}$ –10^{-3} M) was determined at 20 °C from the concentration of the metal ion in the aqueous phase before and after extraction, monitored spectrophotometrically using Arsenazo (III) (2,2′-[1,8 dihydroxy-3,6-di-sulphonaphthalene-2,7-diyl-bis(azo)] bis (benzenearsonic acid)) as colored reagent. The conditions of a standard experiment and the calculation of %E have been previously reported in detail [5].

Spectrophotometric study

The stability constants β defined as concentration ratios (e. g. $[ML_2^{n+}]/([M^{n+}][L]^2$ for a ML_2 complex, where M^{n+} = cation and L = ligand) were determined in methanol and acetonitrile by UV absorption spectrophotometry, at 25 °C and constant ionic strength provided by 0.01 M Et_4NNO_3 according to the procedure already described [20]. The spectra were recorded on a Varian Cary 3 spectrophotometer. The ligand concentrations were *c.a.* 10^{-4} –5×10^{-4} M and the spectra were treated by the program Specfit [21].

Microcalorimetric study

Microcalorimetric experiments were performed using a 2277 Thermal Activity Monitor Microcalorimeter (Thermometric). Titrations were carried out at 25 °C on 2.7 mL of *c.a.* 5×10^{-4}–10^{-3} M of the ligands in methanol or acetonitrile using a 4 mL glass cell. The heats of formation of the complexes were measured after addition of 17×15 mL aliquots of 5×10^{-3}–3×10^{-2} M of europium or uranyl nitrates in the same solvent. Chemical calibration was made by determination of the complexation enthalpy of Ba^{2+} with 18C6 in water or of Rb^+ with 18C6 in methanol, as recommended [22]. The enthalpy of complexation (ΔH) and the stability constants were refined simultaneously from these data using the ligand binding analysis program DIGITAM version 4.1 [23] and after correction for the heat of dilution of the metal salt determined in separate titrations without the ligands. The corresponding values of the entropy of complexation (ΔS) were then calculated from the expression $\Delta G = \Delta H - T\Delta S$, knowing $\Delta G = -RT \ln \beta$.

References

1. Grossi, G., Cecille, L.: New separation chemistry techniques for radioactive waste and other specific applications. In: Cecille, L., Carsarci, M., Pietrelli, L. (eds.) Elsevier, London (1991)
2. Babain, V.V., Shadrin, A.Yu.: Chemical separation technologies and related methods of nuclear wastes management. Kluwer Academic Publishers, The Netherlands (1999)
3. Arnaud-Neu, F., Barboso, S., Byrne, D., Charbonniere, L. J., Schwing-Weill, M. J., Ulrich, G.: Binding of lanthanides(III) and thorium(IV) by phosphorylated calixarenes. American Chemical Society, Symposium Series no 757/Calixarenes for Separations, pp. 150–164. Book Editors Lumetta, G.J., Rogers, R.D., Gopalan, A.S., Chapter 12 (2000)
4. Arnaud-Neu, F., Schwing-Weill, M.J., Dozol, J.F.: Calixarenes for nuclear waste treatment. In: Asfari, Z., Böhmer, V., Harrowfield, J.M., Vicens, J. (eds.) Calixarenes 2001, pp. 642–662. Kluwer Academic Publishers, Dordrecht (2001)
5. Cherenok, S., Kalchenko, V.: Phosphorus-containing calixarenes. Top. Heterocycl. Chem. **20**, 229–273 (2009)
6. Arnaud-Neu, F., Böhmer, V., Dozol, J.F., Gruttner, C., Jakobi, R.A., Mauprivez, O., Rouquette, H., Schwing-Weill, M.J., Simon, N., Vogt, W.: Calixarenes with diphenylphosphoryl acetamide functions at the upper rim. A new class of highly efficient extractants for lanthanides and actinides. J. Chem. Soc., Perkin Trans. **2**, 1175–1182 (1996)
7. Arnaud-Neu, F., Browne, J.K., Byrne, D., Marrs, D.J., McKervey, M.A., O'Hagan, P., Schwing-Weill, M.J., Walker, A.: Extraction and complexation of alkali, alkaline earth and f-element cations by calixaryl phosphine oxides. Chem. Eur. J. **5**, 175–186 (1999)
8. Smirnov, I., Karavan, M., Babain, V., Kvasnitskiy, I., Stoyanov, E., Miroshnichenko, S.: Effect of alkyl substituents on extraction properties and solubility of calix[4]arene dialkylphosphine oxides. Radiochim Acta **95**, 97–102 (2007)
9. Smirnov, I., Karavan, M., Efremova, T.I., Babain, V.: Extraction of Am, Eu, Tc and Pd from nitric acid solutions with phosphorylated calixarenes. Radiochemistry **5**, 423–431 (2007)
10. Matthews, S.E., Saadioui, M., Böhmer, V., Barboso, S., Arnaud-Neu, F., Schwing-Weill, M.J., Garcia Carrera, A., Dozol, J.F.: Conformationally mobile wide rim carbamoylmethylphosphine oxide (CMPO)-calixarenes. J. Prakt. Chem. **341**, 264–273 (1999)
11. Thuery, P., Nierlich, M., Harrowfield, J., Ogden, M.: Phenoxide complexes of f-elements, Calix 2001, In: Asfari, Z. Böhmer, V., Harrowfield, J., Vicens, J. (eds.) Kluwer Academic Publishers, Dordrecht, pp. 561–582 (2001)
12. Guilbaud, P., Wipff, G.: Selective complexation of UO_2^{2+} by the calix[6]arene^{6-} anion: structure and hydration studied by molecular dynamics simulations. J. Incl. Phenom. Mol. Recogn. Chem. **16**, 169–188 (1993). doi:10.1007/BF00709150
13. Barboso, S., Carrera, A.G., Matthews, S.E., Arnaud-Neu, F., Böhmer, V., Dozol, J.F., Rouquette, H., Schwing-Weill, M.J.: Calix[4]arenes with CMPO functions at the narrow rim. Synthesis and extraction properties. J. Chem. Soc. Perkin Trans. **2**, 719–723 (1999)
14. Atamas, L., Klimchuk, O., Rudzevich, V.L., Kalchenko, V., Smirnov, I., Babain, V., Efremova, T., Varnek, A., Wipff, G., Arnaud-Neu, F., Roch, M., Saadioui, M., Böhmer, V.: New Organophosphorus Calix[4]arene Ionophores for Trivalent Lanthanide and Actinide Cations. J. Supramol. Chem. **2**, 421–427 (2002). doi:10.1016/S1472-7862(03)00052-2
15. Klimchuk, O., Atamas, L., Miroshnichenko, V., Kalchenko, V., Smirnov, I., Varnek, A., Wipff, G.: New Wide Rim Phosphomethylated Calix[4]arenes in Extraction of Americium and Europium. J. Incl. Phenom. Macrocycl. Chem. **49**, 47–56 (2004)
16. Vovk, A., Kalchenko, V., Cherenok, S.A., Kukhar, V.P., Muzychka, O.V., Lozynsky, M.O.: Calix[4]arene methylenebisphosphonic acids as calf intestine alkaline phosphatase inhibitors. Org. Biomol. Chem. **2**, 3162–3166 (2004)
17. Kostin, G.A., Borodin, A.O., Torgov, V.G., Kuratyeva, N.V., Naumov, D.Yu., Miroshnichenko, S.I., Kalchenko, V.I.: Monomeric and polymeric dinuclear complexes of Co(II) or Ni(II) with calix[4]arenes tetraphosphine oxide. J. Incl. Phenom. Macrocycl. Chem. **59**, 45–52 (2007)
18. Torgov, V.G., Us, T.V., Korda, T.M., Kostin, G.A., Miroshnichenko, S.I., Klimchuk, O.V., Kalchenko, V.I.: A Ru/Zn synergism in extraction of ruthenium by calixarene phosphine oxides. J. Incl. Phenom. Macrocycl. Chem. **62**, 51–58 (2008)
19. Merck, E.; Méthodes d'analyses complexométriques par les Titriplex, 3ème ed, Darmstadt, Germany
20. Arnaud-Neu, F., Schwing-Weill, M.J., Ziat, K., Cremin, S., Harris, S.J., McKervey, M.A.: Selective alkali and alkaline-earth complexation by calixarene amides. New J. Chem. **15**, 33–37 (1991)
21. Gampp, H., Maeder, M., Meyer, C.J., Zueberbuhler, A.D.: Calculation of equilibrium constants from multiwavelength spectroscopic data-II: Specfit: two user-friendly programs in basic and standard fortran 77. Talanta **32**, 257–264 (1985). doi:10.1016/0039-9140(85)80077-1
22. Arnaud-Neu, F., Delgado, R., Chavez, S.: Critical evaluation of stability constants and thermodynamic functions of metal complexes of crown ethers. Pure Appl. Chem. **75**, 71–102 (2003)
23. Hallen, D.: Data treatment: considerations when applying binding reaction data to a model. Pure Appl. Chem. **65**, 1527–1532 (1993)