Ligands for Eu^{III}, Fe^{III}, Sr^{II}, and UO_2^{II} Based on CMPO-Functionalized Resorcinarene Cavitands; Synthesis and Extraction

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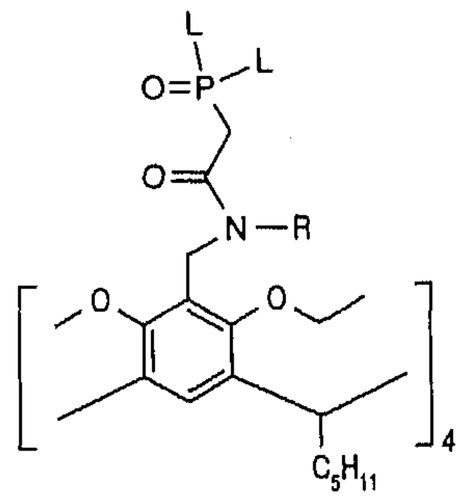
Partially functionalized cavitands (**7a–d**) have been synthesized starting from the tetrakis(bromomethyl)cavitand **6**. New cavitand-based cation ligands, with one to three carbamoylmethylphosphane oxide (CMPO) moieties (**11a–d**), were prepared in good (66–90%) yields. The ligands **11a–d** extract Eu^{III}, but do so less effectively than the tetra-CMPO cavitand **1**. The decreasing number of CMPO groups which result in decreasing extraction percentages for Eu^{III}, also decrease the selectivity of Eu^{III} over that of Fe^{III}, Sr^{II}, and UO_2^{II}. There is a difference in extraction behavior, determined by radio-tracer experiments, between the distal and proximal disubstituted ligands, **11b** and **11c**, respectively. The extraction constants for the 1:1 complex of **11b** and **11c** with Eu(picrate)$_3$ are $K_{ex} = 6.7 \cdot 10^8$ M^{-4} and $3.7 \cdot 10^9$ M^{-4}, respectively.

In a strategy for reducing the volume of radioactive waste, effective separation of the trivalent actinides (americium and curium) is required. Carbamoylmethylphosphoryl [CMP(O)] derivatives are commonly used as organic extractants for the recovery of these trivalent trans-plutonium actinides[1]. In our previous paper[2] we reported the synthesis and extraction of europium, selected as being representative of the trivalent actinides americium and curium[3], by a new type of resorcinarene cavitand ligand with carbamoylmethylphosphonate (CMP) and -phosphane oxide (CMPO) groups (ligands **1–4**, see Scheme 1). Due to the attachment of four CMP(O) moieties to the rigid cavitand frame, and the tight preorganization of the coordinating sites, the efficiency and selectivity [of Eu^{III} over UO_2^{II} and Fe^{III}] of the metal extraction process was improved, compared to that with simple CMP(O) extractants.

Scheme 1. Structure of the tetra-CMP(O)-functionalized cavitands



	R	L
1	H	Ph
2	C_3H_7	Ph
3	H	OEt
4	C_3H_7	OEt

Subsequently, we investigated the influence of the number of ligating sites on the extraction properties and complexation strength. Although in the ligands **1–4** all CMPO groups are associated in the (europium) complex[2], their individual contributions may be different. Furthermore, we observed that ligand **2** extracts Eu^{III} from aqueous solutions that contain an excess of Eu^{III}, in a 1:2 (ligand/cation) complex stoichiometry, indicating Eu^{III} complexation with only two proximally positioned CMPO moieties. Therefore, analogous resorcinarene ligands with less than four CMPO moieties should give more insight into the effects of structural variation on the extraction properties. In this paper we present the synthesis and europium extraction results of resorcinarene-derivatized CMPO ligands, based on partially substituted cavitands.

Results and Discussion

Synthesis

The partially functionalized cavitands **7a–d** have been prepared starting from the (previously described) tetrakis(bromomethyl)cavitand **6**[2] by partial substitution of (a) bromo atom(s) for (a) phthalimido group(s) (Scheme 2)[4]. The four partially functionalized products, the monophthalimido- (**7a**), the distal (or 1,3-bis)phthalimido- (**7b**), the proximal (or 1,2-bis)phthalimido- (**7c**), and the tris(phthalimidomethyl)cavitand **7d**, were formed by the reac-

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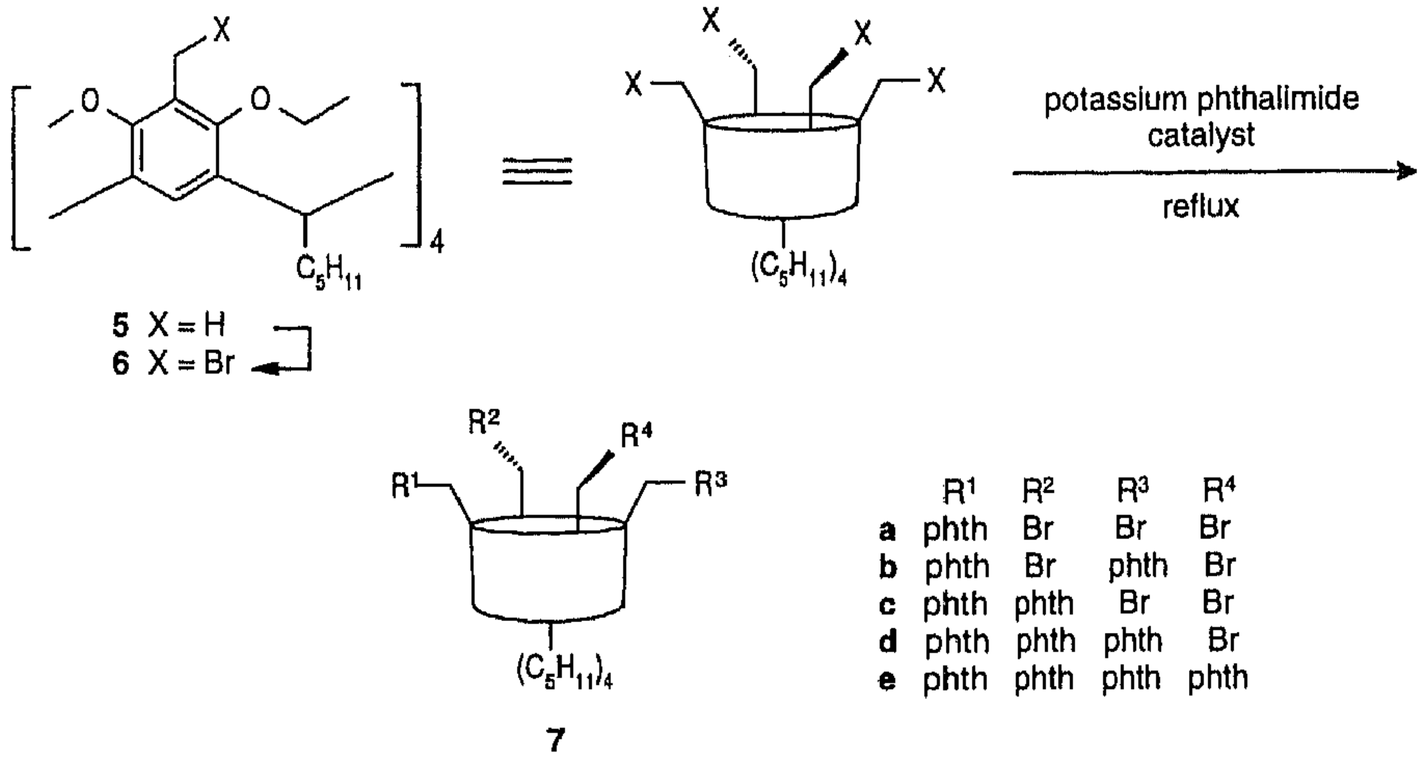
tion of the bromomethylcavitand **6**, with less than four equiv. of potassium phthalimide and tributylhexadecylphosphonium bromide as the phase transfer catalyst. Depending on the reaction conditions, varying ratios of the compounds **7a–d** and, in addition, small amounts of tetrasubstituted derivative **7e**, were formed. Due to the influence of the number of phthalimido moieties on the polarity, the different compounds could be easily separated using column chromatography.

Scheme 2. Synthesis of the partially substituted cavitands



In general, the yields of the partially substituted products **7a–d** are influenced by (i) the solvent and (ii) the number of potassium phthalimide equivalents. When the reaction is carried out in toluene (Table 1; entries 1 and 2) the yield of partially substituted cavitands **7a–d** depends statistically upon the equiv. of potassium phthalimide added. In DMF (entry 3) the introduction of the second phthalimido group is slower, as can be concluded from the low yield of the disubstituted compounds **7b** and **7c**, relative to the mono- and trisubstituted cavitands **7a** and **7d**, respectively. The relative distribution of **7b** and **7c** of 1:2 is in agreement with the statistically expected ratio, which was also found for the reaction in toluene. In acetonitrile (entries 4 and 5), however, the relative distribution of both disubstituted compounds (**7b** and **7c**) is inversed from the statistical 1:2 ratio to a 2–3 fold excess of the distal over the proximal diphthalimido cavitand. This can be explained by the lower solubility of **7b**, when compared to **7c**, inducing partial precipitation. Consequently, most of **7c** reacted further to give the trisubstituted product **7d**.

The cavitand **7b** can be clearly differentiated from the proximally substituted cavitand **7c** by the signals for the methyleneoxy bridge protons in the ^{1}H-NMR spectra. In the spectrum of **7b** only one doublet at $\delta = 6.02$ is present for the (outer) bridge protons, due to the two planes of symmetry, while the spectrum of **7c** (with one plane of symmetry), shows three doublets (ratio 1:1:2) at $\delta = 6.03$, 5.97, and 5.95, respectively. Both the mono- and trisubstituted derivatives (**7a** and **7d**) exhibit two doublets for the (outer) bridge protons.

CMPO-Based Ligands: The CMPO ligating sites were introduced into the partially aminomethyl-substituted cavitands **9a–d** (Scheme 3). Compounds **9a–d** could not be prepared directly from the phthalimido-substituted derivatives **7a–d** as treatment of the phthalimido groups with hydrazine hydrate, in the presence of the bromomethyl groups, would result in intermolecular auto-alkylation of the released amino groups. Therefore, the bromo atom(s) of **7a–d** had to be removed prior to the deprotection of the amino moieties. Treatment of **7a–d** with $NaBH_4$ in DMF at −10°C gave the debrominated phthalimido-substituted cavitands **8a–d** in reasonable to good yields (51–87%)[5,6]. Subsequent treatment of the cavitands **8a–d** with hydrazine hydrate in refluxing ethanol/THF afforded the aminomethyl-methylcavitands **9a–d** in yields of 89–99%[7–9].

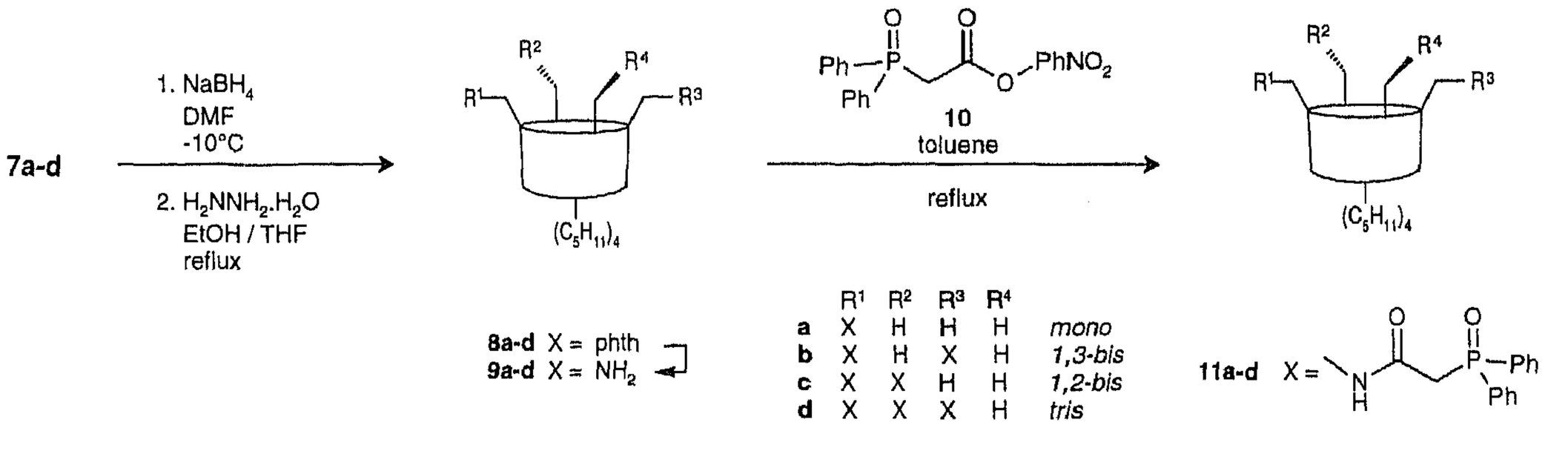
Table 1. Product distribution of partially substituted compounds

Entry	solvent [a,b]	K.phth[c] [equiv]	Time [hours]	Yield[d] [%] 7a	7b	7c	7d	7e	total
1	toluene	2.0	5	28	12	25	8	2	75
2	toluene	2.4	17	7	8	20	37	–[e]	72
3	DMF	2.2	4.5	21	2	5	14	10	52
4	CH_3CN	2.2	4	12	22	7	17	11	69
5	CH_3CN	2.2	5	13	26	11	20	5	75

[a] All reactions were performed at reflux temperature, except for DMF (70°C). – [b] For 1.0 g of starting compound (**6**), 100 ml of solvent was used. – [c] The catalyst was used in 0.1 equiv. to the potassium phthalimide. – [d] Isolated yield. – [e] Product not isolated.

The diphenyl-carbamoylmethylphosphane oxide (Ph_2-CMPO) moieties were introduced by aminolysis of the aminomethyl groups in the cavitands **9a–d** with *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**)[2,10] to give the (diphenyl-*N*-methylcarbamoylmethylphosphane oxide)methylcavitands **11a–d** in yields of 66–90%. In the ^{1}H-NMR spectra all new ligands exhibit the expected number of signals for the aromatic and outer bridge protons, and in ratios that correspond clearly to their structure. The presence of the

Scheme 3. Synthesis of the partially CMPO-functionalized ligands



CMPO moieties is shown by the doublet for the C(O)CH_2P(O) protons around $\delta = 3.25$ ($^2J_P = 12.7$ Hz).

Extractions

In order to study the influence of the number of the ligating moieties, picrate (2,4,6-trinitrophenolate) extractions were carried out with the new ligands[11]. To allow comparison with the tetrasubstituted ligand **1** the same cations were investigated as in our previous study[2]. Europium was selected as a general representative for the trivalent actinides (e.g. americium and curium) and lanthanide group elements[3], and the selectivity for europium over five other elements was studied, viz. sodium, iron [Fe^{III}][12], strontium, cesium[13], and uranium [as UO_2^{II}][14].

Metal Extractions: The results of the extraction experiments with the partially CMPO functionalized ligands **11a–d**, and the tetrasubstituted analogue **1**, are summarized in Table 2 (the extraction properties are expressed as %E, the percentage cation extracted; see the Experimental Section).

Table 2. Extraction of cations with partially CMPO-functionalized ligands

	Percentage of cation extracted, %E[a]				
	1[b]	**11a**	**11b**	**11c**	**11d**
Na^+	<1	<1	<1	<1	<1
Cs^+	<1	<1	<1	<1	<1
Sr^{2+}	80	34	59	85	83
UO_2^{2+}	92	57	95	93	98
Fe^{3+}[c]	55	25	16	64	74
Eu^{3+}	93	31	63	93	98

[a] $[L]_{o,i} = 10^{-3}$ M; $[M^{n+}]_{w,i} = 10^{-4}$ M; $[LiPic]_w = 10^{-2}$ M; $[HNO_3]_w = 10^{-3}$ M; pH = 3.0. – [b] From ref.[2]. – [c] $[L]_{o,i} = 10^{-3}$ M; $[Fe^{3+}]_{w,i} = 10^{-4}$ M; $[LiPic]_w = 10^{-2}$ M; $[LiCl]_w = 0.9 \cdot 10^{-2}$ M; $[HCl]_w = 10^{-3}$ M; pH = 3.0.

All ligands extract the elements Sr^{II}, UO_2^{II}, Fe^{III}, and Eu^{III} and, furthermore, none of the ligands shows any significant affinity for the first row alkali metals Na and Cs. The extraction of Eu^{III} with the cavitands **11a–d** increases with increasing number of CMPO moieties (**1** shows a maxium extraction level, vide infra), with the exception of the proximally substituted compound **11c**. The extraction behavior of **11c** is comparable with that of the trisubstituted cavitand **11d**; **11c** is a (much) better extractant than its distally disubstituted analogue **11b** [exception for UO_2^{II}]. Obviously, two proximally positioned CMPO groups (e.g. **11c**) fulfill the coordination requirements of Eu^{III} better than two distal CMPO moieties (e.g. **11b**). The introduction of an additional (third) CMPO unit (**11d** vs. **11c**) increases the Eu^{III} extraction to a lesser extent. The %E values of the extractable cations have been calculated as distribution coefficients (using eq. 5; see Experimental Section) and their separation factors, compared to Eu^{III}, are presented in Table 3. Comparison of the $S_{Eu/M}$ values reveals that for the ligands **11a–d** the selectivity ($S_{Eu/M}$ values) generally increases with increasing number of CMPO moieties, similar to the increasing %E values. The extraction of Eu^{III} is more sensitive to variation in the number of CMPO groups than that of other elements. Therefore, the higher selectivity is mainly caused by the increasing D_{Eu} values. The three strongest binding ligands (**1**, **11d**, and **11c**) extract both Eu^{III} and UO_2^{II} to essentially the same extent ($S_{Eu/UO_2} \approx 1$).

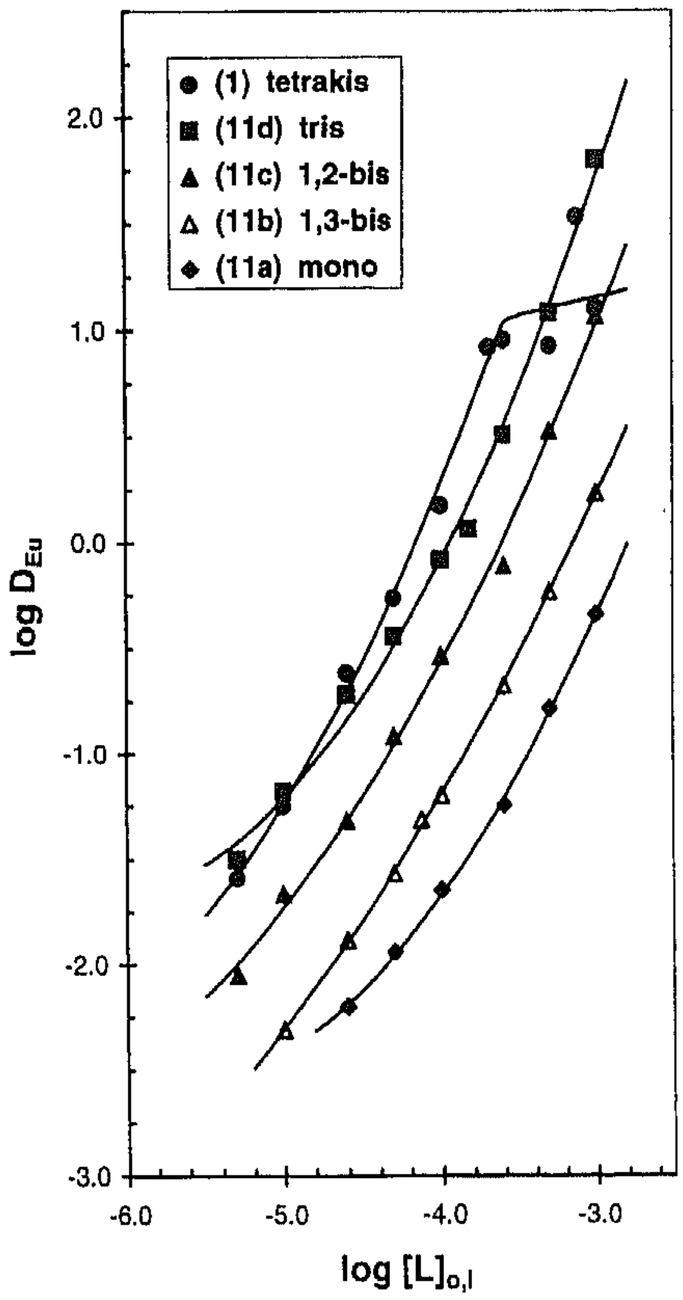
Table 3. Distribution coefficients and separation factors

	Distribution coefficients				Separation factors[a]		
	D_{Sr}	D_{UO_2}	D_{Fe}	D_{Eu}	$S_{Eu/Sr}$	S_{Eu/UO_2}	$S_{Eu/Fe}$
1[b]	4.0	11.5	1.2	14.1	3.5	1.2	12
11a	0.52	1.3	0.33	0.45	0.87	0.34	1.4
11b	1.4	19.0	0.19	1.7	1.2	0.09	8.8
11c	5.7	13.3	1.8	13.0	2.3	0.98	7.3
11d	4.9	49	2.9	46	9.3	0.93	16

[a] $S_{a/b} = D_a/D_b$. – [b] From ref.[2].

Extraction Constants: The dependence of D_{Eu} on $[L]_{o,i}$, the initial ligand concentration, is shown in Figure 1 as a plots of log D_{Eu} as function of log $[L]_{o,i}$. The graphs exhibit a curve where generally the curvature is more pronounced with increasing strength of the extractant, while the strongest extractant (tetra-CMPO cavitand **1**) reaches a maximum extraction (distribution). The trends in curvature of the graphs can be attributed to the presence of complexes with different stoichiometries, viz. both 1:1 and 1:2 (host/guest ratio) complexes. This behavior was also found for the tetrasubstituted CMP(O) resorcinarene ligands[2]. In the low ligand concentration region ($[L]_{o,i} < 10^{-4}$ M) the curvature of the plots of **11a** and, especially, **11d** are more pronounced. In spite of the low organic concentrations, this

Figure 1. Plots of log D_{Eu} vs. log $[L]_{o,i}$; $[Eu^{3+}]_{w,i} = 10^{-4}$ M, $[LiPic]_w = 10^{-2}$ M, $[HNO_3]_w = 10^{-3}$ M, pH = 3.0



might be explained by formation of aggregates leading to a slightly increased distribution coefficient.

The extraction coefficients (K_{ex}) for the 1:1 complexes have been calculated from eq. 3 (see Experimental Section), as K_{ex} cannot directly be determined from log D vs. log [L] plots[2]. The K_{ex} values (summarized in Table 4) underline the correlation found between the number of CMPO groups in the cavitand ligands and the level of the extraction. The significant difference between both disubstituted ligands is also reflected in their K_{ex} values. The distally substituted ligand **11c** is a 5.5 times stronger complexant for Eu^{III} than the proximally substituted ligand **11b**. The possibility of intramolecular association between the two CMPO moieties in **11b**, resulting in a lower extraction constant of **11b** (compared to **11c**), can be excluded. Due to the smaller intramolecular CMPO distance in **11c** (compared to **11b**) this effect would be stronger for **11c**, resulting in a lower extraction constant, the opposite of what is observed. Furthermore, the complexation with the tris-CMPO ligand **11d** is four times stronger than with **11c** (but 22 times stronger than with **11b**), while decreasing the number of CMPO moieties from four to three has a smaller effect on the complexation strength (e.g. **11d** is a 2.5 times weaker ligand than the tetrasubstituted ligand **1**). Obviously the individual contributions of the CMPO moieties are not equally essential for the complex formation and strength.

Table 4. Extraction constants of 1:1 complexes

	$E^{[a]} \times 10^2$	K_{ex} [M^{-4}]
tetrakis-**1**[b]	60	$3.7 \cdot 10^{10}$
mono-**11a**	2.2	$2.3 \cdot 10^{8}$
1,3-bis-**11b**	6.0	$6.7 \cdot 10^{8}$
1,2-bis-**11c**	22	$3.7 \cdot 10^{9}$
tris-**11d**	46	$1.5 \cdot 10^{10}$

[a] $[L]_{o,i} = 10^{-4}$ M; $[Eu^{3+}]_{w,i} = 10^{-4}$ M; $[LiPic]_w = 10^{-2}$ M; $[HNO_3]_w = 10^{-3}$ M; pH = 3.0. – [b] From ref.[2].

Conclusions

In this paper we present the synthesis of the partially functionalized cavitands **7a–d** starting from tetrakis(bromomethyl)cavitand **6**. Variation in the relative product distribution is achieved by changing the reaction conditions. The new CMPO ligands **11a–d**, with one to three ligating sites, were prepared in good yields (66–90%). Compared to the tetrakis-CMPO cavitand **1**, the partially CMPO-substituted ligands **11a–d** are less effective extractants for Eu^{III}, as shown by the values of the extraction constants. The difference in extraction behavior of both disubstituted ligands is striking (the K_{ex} of **11c** is 5.5 times larger than the K_{ex} of **11b**), illustrating the effect of steric preorganization. The separation factor for the extraction of Eu^{III} over Sr^{II}, UO_2^{II}, and Fe^{III} decreased going from tris- (**11d**) to mono-CMPO ligand (**11a**), mainly caused by relatively faster decreasing D_{Eu} values.

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Experimental Section

Materials: THF was freshly distilled from Na/benzophenone before use and DMF was dried over molecular sieves (3/4 Å) for at least 3 d. For synthetic uses CH_2Cl_2 was distilled from $CaCl_2$ and kept on molecular sieves (3/4 Å), while p.a. CH_2Cl_2 was used for the extraction experiments. Toluene was distilled from sodium and kept on molecular sieves (3/4 Å). Other chemicals were of reagent grade and used without further purification. Hexanes refer to a petroleum ether isomer mixture with a boiling range between 60–80°C.

Isotopes: The ^{22}Na, ^{59}Fe, and ^{90}Sr isotope solutions were purchased from Amersham (UK). The ^{137}Cs and ^{152}Eu isotope solutions were IPL (Burbank, California, USA) products, while UO_2 (^{238}U, 20% enriched with ^{235}U) was used from ECN stocks.

Synthesis: All reactions were carried out under an argon atmosphere, unless otherwise stated. Flash column chromatography was performed with Merck silica gel 60 (0.040–0.063 mm, 230–400 mesh) and Sephadex column chromatography was performed using Pharmicia BioTech Sephadex LH-20. Melting points were determined with a Reichert melting point apparatus and are uncorrected. Mass (FAB) spectra were recorded with a Finnigan MAT 90 spectrometer using *m*-nitrobenzyl alcohol as a matrix. The ^1H-

NMR and ^{13}C-NMR spectra (250 MHz and 62.5 MHz) were recorded on a Bruker AC 250 spectrometer in $CDCl_3$ at ambient tem., and the chemical shifts were expressed relative to $CDCl_3$ (δ_H = 7.26 and δ_C = 76.91). Elemental analyses were performed with a Model 1106 Carlo Erba Strumentazione Elemental Analyzer, and the presence of solvent molecules in the analytical samples was confirmed by ^{1}H-NMR spectroscopy.

Compounds **5**[2], **6**[2], **10**[10], and lithium picrate[2] were prepared according to literature procedures. The synthesis and characterization of the tetrasubstituted derivatives **1**–**4**, and **7e** have been described elsewhere[2].

Typical Procedure for the Preparation of Partially Phthalimido-Substituted Cavitands: A solution of tetrakis(bromomethyl)cavitand **6** (5.0 g, 4.2 mmol), potassium phthalimide (1.71 g, 9.3 mmol) and hexadecyltributylphosphonium bromide (0.56 g, 1.09 mmol) in CH_3CN (500 ml) was refluxed for 6 h. After evaporation of the solvent the residue was dissolved in CH_2Cl_2 (200 ml), washed with 2 M NaOH (3 × 50 ml) and dried over $MgSO_4$. The partially substituted products were isolated after flash column chromatography (SiO_2, hexanes/EtOAc ratio 80:20–40:60).

Tris(bromomethyl)phthalimidomethylcavitand (**7a**): General yield[15]: 12–13%, m.p. 285–287°C (hexanes/EtOAc). – MS, *m/z* (%): 1255.4 (15%) [M^+]. – ^{1}H NMR: δ = 7.83–7.78 and 7.74–7.69 (2 m, 2:2H, phthalimido), 7.12, 7.09 (2 s, 3:1H, ArH), 6.03, 6.00 (2 d, 2:2H, J = 6.6 Hz, outer OCH_2O), 4.77, 4.74 [2 t, 2:2H, J = 8.0 Hz, $CH(CH_2)_4$], 4.65 (s, 2H, $ArCH_2$phth), 4.58, 4.55 (2 d, 2:2H, J = 7.0 Hz, inner OCH_2O), 4.50, 4.38 (2 s, 4:2H, $ArCH_2Br$), 2.3–2.05 (m, 8H, $CHCH_2$), 1.4–1.15 [m, 24H, $CHCH_2(CH_2)_3$], 0.93–0.84 (m, 12H, CH_3). – ^{13}C NMR: δ = 167.9 [s, NC(O)C], 153.9, 153.8, 153.7, 153.4 (s, $ArCOCH_2O$), 138.2, 138.1, 138.0, 137.8 (s, ArCCH), 133.8, 132.1, 123.3 (d, s, s, phthalimido), 124.5 (s, $ArCCH_2Br$), 122.2 (s, $ArCCH_2$phth), 121.1, 120.1 (d, ArCH), 99.2 (t, OCH_2O), 36.9 (d, ArCHAr). – $C_{64}H_{72}Br_3NO_{10}$ (1255.0): C 61.25, H 5.78, N 1.12; found C 61.45, H 6.02, N 1.28.

1,3-Bis(bromomethyl)-2,4-bis(phthalimidomethyl)cavitand (**7b**): General yield[15]: 22–26%, m.p. 224°C (hexane/EtOAc). – MS, *m/z* (%): 1320.8 (30%) [M^+]. – ^{1}H NMR: δ = 7.83–7.78 and 7.74–7.69 (2 m, 4:4H, phthalimido), 7.10, 7.08 (2 s, 2:2H, ArH), 6.02 (d, 4H, J = 7.4 Hz, outer OCH_2O), 4.71 [t, 4H, J = 7.9 Hz, $CH(CH_2)_4$], 4.63 (s, 4H, $ArCH_2$phth), 4.57 (d, 4H, J = 7.5 Hz, inner OCH_2O), 4.55 (s, 4H, $ArCH_2Br$), 2.35–2.19, 2.15–1.95 (2 m, 4:4H, $CHCH_2$), 1.45–1.15 [m, 24H, $CHCH_2(CH_2)_3$], 0.87 (t, 12H, J = 6.8 Hz, CH_3). – ^{13}C NMR: δ = 167.9 [s, NC(O)], 154.0, 153.7 (s, $ArCOCH_2O$), 138.1, 137.7 (s, ArCCH), 133.8, 132.2, 123.3 (d, s, d, phthalimido), 124.5, 121.8 (s, $ArCCH_2$), 121.2, 120.1 (d, ArCH), 99.3 (t, OCH_2O), 36.9 (d, ArCHAr), 23.2 (t, $ArCH_2Br$). – $C_{72}H_{76}Br_2N_2O_{12}$ (1321.2): calcd. C 65.46, H 5.80, N 2.12; found C 65.06, H 6.03, N 2.12.

1,2-Bis(bromomethyl)-3,4-bis(phthalimidomethyl)cavitand (**7c**): General yield[15]: 7–11%, m.p. 272–274°C (hexanes/EtOAc). – MS, *m/z* (%): 1320.6 (45%) [M^+]. – ^{1}H NMR: δ = 7.83–7.78 and 7.74–7.69 (2 m, 4:4H, phthalimido), 7.12, 7.09 (2 s, 2:2H, ArH), 6.03, 5.97, 5.95 (3 d, 1:1:2H, J = 7.4 Hz, outer OCH_2O), 4.77–4.65 [m, 8H, $CH(CH_2)_4$, 4H, $ArCH_2$phth], 4.60, 4.58, 4.55 (3 d, 4H, J = 7.5 Hz, inner OCH_2O), 4.50 (s, 4H, $ArCH_2Br$), 2.35–2.05 (m, 8H, $CHCH_2$), 1.4–1.15 [m, 24H, $CHCH_2(CH_2)_3$], 0.87 (t, 12H, J = 7.0 Hz, CH_3). – ^{13}C NMR: δ = 167.9 [s, NC(O)], 154.1, 153.8, 153.7, 153.6 (s, $ArCOCH_2O$), 138.0, 137.8 (s, ArCCH), 133.8, 132.2, 123.3 (d, s, d, phthalimido), 124.5, 121.6 (s, $ArCCH_2$), 121.0, 120.1 (d, ArCH), 99.3 (t, OCH_2O), 36.9 (d, ArCHAr), 23.5 (t, $ArCH_2Br$). – $C_{72}H_{76}Br_2N_2O_{12} \cdot C_6H_{12}$ (1405.4): calcd. C 66.57, H 6.45, N 1.99; found C 66.64, H 6.61, N 1.97.

Bromomethyltris(phthalimidomethyl)cavitand (**7d**): General yield[15]: 17–23%, m.p. 154–156°C (EtOAc/hexanes). – MS, *m/z* (%): 1387.5 (30) [M^+]. – ^{1}H NMR: δ = 7.81–7.76 and 7.71–7.66 (2 m, 6:6H, phthalimido), 7.09, 7.06 (2 s, 1:3H, ArH), 5.95, 5.81 (2 d, 2:2H, J = 6.4 Hz, outer OCH_2O), 4.69 [t, 4H, J = 8.2 Hz, $CH(CH_2)_4$], 4.65 (s, 6H, $ArCH_2$phth), 4.57, 4.41 (2 d, 2:2H, J = 7.2 Hz, inner OCH_2O), 4.52 (s, 2H, $ArCH_2Br$), 2.3–2.05 (m, 8H, $CHCH_2$), 1.4–1.15 [m, 24H, $CHCH_2(CH_2)_3$], 0.85 (t, J = 7.0 Hz, 12H, CH_3). – ^{13}C NMR: δ = 167.9 [s, NC(O)], 154.0, 153.8, 153.6 (s, $ArCOCH_2O$), 138.1, 137.9, 137.8 (s, ArCCH), 133.9, 132.1, 123.3 (d, s, d, phthalimido), 124.5, 121.5 (s, $ArCCH_2$), 121.1, 120.4 (d, ArCH), 99.5 (t, OCH_2O), 60.4 (t, $ArCH_2$phth), 36.9 (d, ArCHAr), 23.5 (t, $ArCH_2Br$). – $C_{80}H_{80}BrN_3O_{14} \cdot 2\ H_2O$ (1423.4): calcd. C 67.49, H 5.95, N 2.95; found C 67.63, H 6.08, N 2.72.

General Procedure for the Debromination of Partially Bromomethylcavitands: A solution of the partially bromomethyl-phthalimidomethylcavitand in DMF was cooled to –10°C (brine/ice bath) and $NaBH_4$ was added in portions. The progress of the reaction was followed with TLC until almost all the starting material had disappeared (60–90 min). After the addition of CH_2Cl_2 the reaction was quenched with 2 M HCl, and the aqueous layer was, additionally, extracted twice with CH_2Cl_2. The collected organic layers were washed with 2 M HCl (3 ×) and dried over Na_2SO_4. The solvent was removed in vacuo and the crude product was purified by flash column chromatography.

Trimethylphthalimidomethylcavitand (**8a**) was prepared starting from the tris(bromomethyl)phthalimidomethylcavitand **7a** (200 mg, 159 μmol) and $NaBH_4$ (0.27 g, 7.2 mmol) in DMF (5 ml). After stirring the reaction mixture for 80 min and chromatography (SiO_2, EtOAc/hexanes, 30:70) **8a** was isolated as a white foam. Yield: 94 mg (58%), m.p. 126–128°C (CH_2Cl_2). – MS, *m/z* (%): 1018.2 (100) [M^+]. – ^{1}H NMR: δ = 7.83–7.78 and 7.74–7.69 (2 m, 2:2H, phthalimido), 7.09, 6.96 (2 s, 1:3H, ArH), 5.86, 5.79 (2 d, 2:2H, J = 6.9 Hz, outer OCH_2O), 4.75, 4.22 [2 t, 2:2H, J = 8.0 Hz, $CH(CH_2)_4$], 4.75 (s, 2H, $ArCH_2$phth), 4.33, 4.26 (2 d, 2:2H, J = 7.0 Hz, inner OCH_2O), 2.4–2.05 (m, 8H, $CHCH_2$), 1.99, 1.91 (2 s, 3:6H, $ArCH_3$), 1.4–1.15 [m, 24H, $CHCH_2(CH_2)_3$], 0.89 (t, 12H, J = 6.6 Hz, CH_3). – ^{13}C NMR: δ = 167.8 [s, NC(O)C], 153.4 (s, $ArCOCH_2O$), 138.0, 137.2 (s, ArCCH), 133.8, 132.1, 123.3 (d, s, d, phthalimido), 123.4 ($ArCCH_3$), 121.0 ($ArCCH_2$phth), 119.8, 117.3 (d, ArCH), 99.2 (t, OCH_2O), 37.0 (d, ArCHAr), 10.4 (q, $ArCH_3$). – $C_{64}H_{75}NO_{10}$ (1018.3): calcd. C 75.49, H 7.42, N 1.38; found C 75.48, H 7.63, N 1.49.

1,3-Dimethyl-2,4-bis(phthalimidomethyl)cavitand (**8b**) was prepared starting from 1,3-bis(bromomethyl)-2,4-bis(phthalimidomethyl)cavitand **7b** (500 mg, 0.378 mmol) and $NaBH_4$ (72 mg, 1.89 mmol) in DMF (10 ml). After stirring the reaction mixture for 65 min and chromatography (SiO_2, EtOAc/hexanes, 50:50) **8b** was isolated as a white foam. Yield: 0.223 g (51%), m.p. 303–305°C (EtOAc/hexanes). – MS, *m/z* (%): 1162.4 (100) [M^+]. – ^{1}H NMR: δ = 7.84–7.77 and 7.76–7.68 (2 m, 4:4H, phthalimido), 7.08, 6.95 (2 s, 2:2H, ArH), 5.81 (d, 4H, J = 7.0 Hz, outer OCH_2O), 4.74 (s, 4H, $ArCH_2$phth), 4.72 [t, 4H, J = 8.9 Hz, $CH(CH_2)_4$], 4.33 (d, 4H, J = 7.1 Hz, inner OCH_2O), 2.35–2.18, 2.18–1.95 (2 m, 4:4H, $CHCH_2$), 1.90 (s, 6H, $ArCH_3$), 1.50–1.20 (m, 24H, $CHCH_2(CH_2)_3$], 0.88 (t, 12H, J = 6.8 Hz, CH_3). – ^{13}C NMR: δ = 168.1 [s, NC(O)], 153.7, 153.5 (s, $ArCOCH_2O$), 138.5, 137.3 (s, ArCCH), 134.0, 132.0, 123.3 (d, s, d, phthalimido), 123.8, 120.9 (s, $ArCCH_2$), 120.6, 117.0 (d, ArCH), 99.1 (t, OCH_2O), 37.0 (d, ArCHAr), 32.8 (t, $ArCH_2$phth), 10.4 (q, $ArCH_3$). – $C_{72}H_{78}N_2O_{12}$

· H_2O (1181.4): calcd. C 73.20, H 6.83, N 2.37; found C 73.57, H 6.78, N 2.56.

1,2-Dimethyl-3,4-bis(phthalimidomethyl)cavitand (**8c**) was prepared starting from 1,2-bis(bromomethyl)-3,4-bis(phthalimidomethyl)cavitand **7c** (0.59 g, 0.48 mmol) and $NaBH_4$ (84 mg, 2.23 mmol) in DMF (15 ml). After stirring the reaction mixture for 70 min and chromatography (SiO_2, hexanes/EtOAc, 70:30) **8c** was isolated as a white foam. Yield: 0.45 g (87%), m.p. 283−285°C (EtOAc/hexanes). − MS, *m/z* (%): 1162.5 (100) [M^+]. ^{1}H NMR: δ = 7.78−7.73 and 7.69−7.64 (2 m, 4:4H, phthalimido), 7.07, 6.94 (2 s, 2:2H, ArH), 5.82, 5.75 (2 d, 1:3H, *J* = 6.9 Hz, outer OCH_2O), 4.76−4.60 [m, 8H, C*H*$(CH_2)_4$], 4.66 (s, 4H, $ArCH_2$phth), 4.36−4.29 (m, 4H, inner OCH_2O), 2.3−2.0 (m, 8H, CHC*H*$_2$), 1.67 (s, 6H, $ArCH_3$), 1.45−1.15 [m, 24H, $CHCH_2(CH_2)_3$], 0.85 (t, 12H, *J* = 6.8 Hz, CH_3). − ^{13}C NMR: δ = 171.0, 167.9 [s, NC(O)], 153.8, 153.7, 153.5, 153.4 (s, Ar*C*OCH_2O), 138.5, 138.0, 137.8, 137.3, 137.2 (s, Ar*C*CH), 134.0, 132.0, 123.3 (d, s, d, phthalimido), 123.9, 121.1 (s, Ar*C*CH_2), 120.4, 117.2 (d, ArCH), 99.9, 99.1, 98.4 (t, OCH_2O), 37.0, 36.9 (d, ArCHAr), 32.7 (t, $ArCH_2$phth), 10.3 (q, $ArCH_3$). − $C_{72}H_{78}N_2O_{12}$ · 2.5 H_2O (1208.4): calcd. C 71.56, H 6.92, N 2.32; found C 71.68, H 6.14, N 2.43.

Methyltris(phthalimidomethyl)cavitand (**8d**) was prepared starting from bromomethyltris(phthalimidomethyl)cavitand **7d** (75 mg, 54.1 μmol) and $NaBH_4$ (31 mg, 0.81 mmol) in DMF (3 ml). After stirring the reaction mixture for 80 min followed by chromatography (SiO_2, EtOAc/hexanes, 60:40) **8b** was isolated as a white foam. Yield: 52 mg (73%), m.p. 155−157°C (CH_2Cl_2/hexanes). − MS, *m/z* (%): 1309.0 (100) [M^+ + H]. − ^{1}H NMR: δ = 7.83−7.76 and 7.72−7.67 (2 m, 6:6H, phthalimido), 7.06, 6.93 (2 s, 3:1H, ArH), 5.98, 5.95 (2 d, 2:2H, *J* = 7.4 Hz, outer OCH_2O), 4.68 [t, 4H, *J* = 7.9 Hz, C*H*$(CH_2)_4$], 4.66 (s, 6H, $ArCH_2$phth), 4.37 (d, 4H, *J* = 7.0 Hz, inner OCH_2O), 2.35−2.0 (m, 8H, CHC*H*$_2$), 1.90 (s, 3H, $ArCH_3$), 1.45−1.15 [m, 24H, $CHCH_2(CH_2)_3$], 0.86 (t, *J* = 6.8 Hz, 12H, CH_3). − ^{13}C NMR: δ = 168.0 [s, NC(O)], 153.9, 153.8, 153.7, 153.6 (s, Ar*C*OCH_2O), 138.1, 137.7, 137.3 (s, Ar*C*CH), 134.0, 132.1, 132.0, 123.3 (d, s, d, phthalimido), 123.9 (s, Ar*C*CH_3), 121.0 (s, Ar*C*CH_2phth), 120.3, 116.4 (d, ArCH), 99.8, 99.0 (t, OCH_2O), 36.9 (d, ArCHAr), 32.8 (t, $ArCH_2$phth), 10.5 (q, $ArCH_3$). − $C_{80}H_{81}N_3O_{14}$ · 2 H_2O (1344.6): calcd. C 71.46, H 6.37, N 3.13; found C 71.63, H 6.17, N 3.10.

General Procedure for the Deprotection of Amino Groups; Formation of **9a−d**: A solution of the partially methylphthalimidomethylcavitand and hydrazine hydrate in a 9:1 mixture of EtOH and THF was refluxed for 4−8 h. After adding concentrated HCl the reaction mixture was refluxed for an additional 1 h. The solvents were removed in vacuo and the precipitate dissolved in CH_2Cl_2, washed with 2 M NaOH (2 ×), H_2O (3 ×), and dried over Na_2SO_4.

Aminomethyltrimethylcavitand (**9a**) was prepared by reaction of trimethylphthalimidomethylcavitand **8a** (89 mg, 87.4 μmol) and hydrazine hydrate (0.09 ml, 0.44 mmol) in a mixture of EtOH (9 ml) and THF (1 ml) for 7 h. White foam. Yield: 75 mg (97%), m.p. 119−121°C (CH_2Cl_2). − MS, *m/z* (%): 871.5 (100) [M^+ − NH_2, calcd. for $C_{56}H_{73}NO_8$ − NH_2]. − ^{1}H NMR: δ = 7.08, 6.95 (2 s, 1:3H, ArH), 5.91, 5.87 (2 d, 2:2H, *J* = 7.0 Hz, outer OCH_2O), 4.76 [t, 4H, *J* = 8.0 Hz, C*H*$(CH_2)_4$], 4.33, 4.29 (2 d, 2:2H, *J* = 7.0 Hz, inner OCH_2O), 3.71 (s, 2H, $ArCH_2NH_2$), 2.25−2.10 (m, 8H, CHC*H*$_2$), 2.00, 1.96 (2 s, 3:6H, $ArCH_3$), 1.5−1.3 [m, 24H, $CHCH_2(CH_2)_3$], 0.91 (t, 12H, *J* = 6.5 Hz, CH_3). − ^{13}C NMR: δ = 153.4, 153.3, 153.0 (s, Ar*C*OCH_2O), 138.4, 138.0, 137.8, 137.5 (s, Ar*C*CH), 128.7 (s, Ar*C*CH_2), 123.9, 123.7 (s, Ar*C*CH_3), 119.5 (d, (CH_2)Ar*C*H), 117.5, 117.3 [d, (CH_2)Ar*C*H], 99.2, 98.4 (t, OCH_2O), 53.4 (t, $ArCH_2NH_2$), 37.0 (d, ArCHAr).

1,3-Bis(aminomethyl)-2,4-dimethylcavitand (**9b**) was prepared by the reaction of the 1,3-dimethyl-2,4-bis(phthalimidomethyl)cavitand **8b** (0.09 g, 0.077 mmol) and hydrazine hydrate (0.04 ml, 0.77 mmol) in a mixture of EtOH (9 ml) and THF (1 ml) for 4 h. Redissolving and evaporating the crude reaction mixture from CH_2Cl_2 (3 × 25 ml) afforded **9b** as a white foam. Yield: 0.07 g (99%), m.p. 140−142°C (CH_2Cl_2). − MS, *m/z* (%): 886.9 (100) [M^+ − NH_2, calcd. for $C_{56}H_{74}N_2O_8$ − NH_2]. − ^{1}H NMR: δ = 7.06, 6.96 (2 s, 2:2H, ArH), 5.87 (d, 4H, *J* = 6.8 Hz, outer OCH_2O), 4.75 [t, 4H, *J* = 7.9 Hz, C*H*$(CH_2)_4$], 4.33 (d, 4H, *J* = 7.0 Hz, inner OCH_2O), 3.70 (s, 4H, $ArCH_2NH_2$), 2.25−2.10 (m, 8H, CHC*H*$_2$), 1.94 (s, 6H, $ArCH_3$), 1.5−1.3 [m, 24H, $CHCH_2(CH_2)_3$], 0.91 (t, 12H, *J* = 6.5 Hz, CH_3). − ^{13}C NMR: δ = 153.4, 153.0 (s, Ar*C*OCH_2O), 138.4, 137.6 (s, Ar*C*CH), 128.1 (s, Ar*C*CH_2NH_2), 123.8 (s, Ar*C*CH_3), 119.5, 117.3 (d, ArCH), 99.1 (t, OCH_2O), 37.0 (d, ArCHAr), 35.5 (t, $ArCH_2NH_2$).

1,2-Bis(aminomethyl)-3,4-dimethylcavitand (**9c**) was prepared by the reaction of the 1,2-dimethyl-3,4-bis(phthalimidomethyl)cavitand **8c** (0.24 g, 0.21 mmol) and hydrazine hydrate (0.20 ml, 4.13 mmol) in a mixture of EtOH (18 ml) and THF (2 ml) for 4.5 h. White foam. Yield: 0.07 g (98%), m.p. 169−171°C (CH_2Cl_2). − MS, *m/z* (%): 857.3 (100) [M^+ − CH_2NH_2 − NH_2, calcd. for $C_{56}H_{74}N_2O_8$ − CH_2NH_2 − NH_2]. − ^{1}H NMR: δ = 7.05, 6.95 (2 s, 2:2H, ArH), 5.92, 5.89, 5.86 (3 d, 1:2:1H, *J* = 6.9 Hz, outer OCH_2O), 4.75 [t, 4H, *J* = 8.1 Hz, C*H*$(CH_2)_4$], 4.35−4.30 (m, 4H, inner OCH_2O), 3.63 (s, 4H, $ArCH_2NH_2$), 2.25−2.10 (m, 8H, CHC*H*$_2$), 1.97 (s, 6H, $ArCH_3$), 1.5−1.3 [m, 24H, $CHCH_2(CH_2)_3$], 0.91 (t, 12H, *J* = 6.8 Hz, CH_3). − ^{13}C NMR: δ = 153.4, 153.3, 153.0, 152.8 (s, Ar*C*OCH_2O), 138.5, 138.1, 137.9, 137.6, 137.5 (s, Ar*C*CH), 128.9 (s, Ar*C*CH_2NH_2), 123.9 (s, Ar*C*CH_3), 119.3, 117.2 (d, ArCH), 99.3, 98.9, 98.3 (t, OCH_2O), 37.0 (d, ArCHAr), 36.0 (t, $ArCH_2NH_2$).

Tris(aminomethyl)methylcavitand (**9d**) was prepared by reaction of methyltris(phthalimidomethyl)cavitand **8d** (109 mg, 83.3 μmol) and hydrazine hydrate (0.12 ml, 2.5 mmol) in a mixture of EtOH (9 ml) and THF (1 ml) for 8 h. White foam. Yield: 68 mg (89%), m.p. 139−141°C (CH_2Cl_2). − MS, *m/z* (%): 844.3 (100) [M^+ − 2 CH_2NH_2 − NH_2 + H, calcd. for $C_{56}H_{75}N_3O_8$ − 2 CH_2NH_2 − NH_2 + H]. − ^{1}H NMR: δ = 7.04, 6.95 (2 s, 3:1H, ArH), 5.61, 5.88 (2 d, 2:2H, *J* = 6.4 Hz, outer OCH_2O), 4.75 [t, 4H, *J* = 8.0 Hz, C*H*$(CH_2)_4$], 4.33 (d, 4H, *J* = 6.8 Hz, inner OCH_2O), 3.63, 3.58 (2 s, 4:2H, $ArCH_2NH_2$), 2.25−2.10 (m, 8H, CHC*H*$_2$), 1.95 (s, 3H, $ArCH_3$), 1.45−1.2 [m, 24H, $CHCH_2(CH_2)_3$], 0.91 (t, 12H, *J* = 6.5 Hz, CH_3). − ^{13}C NMR: δ = 153.4, 153.1, 153.0, 152.9 (s, Ar*C*OCH_2O), 138.5, 138.2, 138.0, 137.6 (s, Ar*C*CH), 129.1 (s, Ar*C*CH_2NH_2), 123.9 (s, Ar*C*CH_3), 119.1, 117.2 (d, ArCH), 99.3, 98.9 (t, OCH_2O), 37.0 (d, ArCHAr), 36.0 (t, $ArCH_2NH_2$).

General Procedure for the Amidation with p-Nitrophenyl (Diphenylphosphoryl)acetate (**10**): A solution of the partially aminomethyl-cavitand and *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**) in toluene was refluxed for 5−11 h. Subsequently, the reaction mixture was cooled to room temp. and the solvent removed in vacuo. The residue was dissolved in CH_2Cl_2 (25 ml), and washed with 5% $NaHCO_3$ (3 × 10 ml), 1 M HCl (10 ml), H_2O (10 ml) and dried over Na_2SO_4. The residue was purified by column chromatography (Sephadex LH-20, MeOH/CH_2Cl_2, 1:1) to give **11a−d** as slightly yellow powders.

(Diphenyl-N-methyl-carbamoylmethylphosphane oxide)trimethylcavitand (**11a**) was prepared by the reaction of the aminomethyltrimethylcavitand **9a** (0.25 g, 0.28 mmol) and *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**) (0.17 g, 0.45 mmol) in toluene (15 ml) for 6 h. Yield 0.21 g (66%), m.p. 116−118°C (CH_2Cl_2/MeOH).

– MS, *m/z* (%): 1152.6 (100) [M^+ + Na]. – ^{1}H NMR: δ = 7.71–7.63 and 7.59–7.45 (2 m, 4:6H, phenyl), 7.22 (t, 1H, NH), 7.10, 6.97 (2 s, 1:3H, ArH), 5.87, 5.74 (2 d, 2:2H, *J* = 7.2 Hz, outer OCH_2O), 4.76, 4.72 [2 t, 2:2H, *J* = 8.1 Hz, $CH(CH_2)_4$], 4.35–4.25 (m, 4H, inner OCH_2O, 2H, $ArCH_2NH$), 3.24 [d, 2H, *J* = 12.7 Hz, $C(O)CH_2P(O)$], 2.25–2.1 (m, 8H, $CHCH_2$), 1.98 (s, 9H, $ArCH_3$), 1.5–1.25 [m, 24H, $CHCH_2(CH_2)_3$], 0.90 (t, 12H, *J* = 6.9 Hz, CH_3). – ^{13}C NMR: δ = 164.4, 164.3 [s, NC(O)], 153.8, 153.4, 153.3 (s, $ArCOCH_2O$), 138.4, 138.0, 137.9, 137.4 (s, ArCCH), 132.7–128.6 (P-phenyl), 123.9, 123.8 (s, $ArCCH_3$), 122.9 (s, $ArCCH_2$), 120.5, 117.4, 117.2 (d, ArCH), 99.6, 98.5 (t, OCH_2O), 38.7 [dt, *J* = 273 Hz, $C(O)CH_2P(O)$], 37.0 (d, ArCHAr), 34.5 (t, $ArCH_2NH$), 10.4, 10.3 (q, $ArCH_3$). – $C_{70}H_{84}NO_{10}P \cdot H_2O$ (1148.4): calcd. C 73.21, H 7.55, N 1.22; found C 73.39, H 7.59, N 1.39.

1,3-Bis(diphenyl-N-methylcarbamoylmethylphosphane oxide)-2,4-dimethylcavitand (**11b**) was prepared by the reaction of 1,3-bis(aminomethyl)-2,4-dimethylcavitand **9b** (0.25 g, 0.28 mmol) and *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**) (0.48 g, 0.91 mmol) in toluene (25 ml) for 5 h. Yield 321 mg (84%), m.p. 130–132°C (CH_2Cl_2/MeOH). – MS, *m/z* (%): 1387.8 (65) [M^+ + H]. – ^{1}H NMR: δ = 7.72–7.64 and 7.58–7.43 (2 m, 8:12H, phenyl), 7.31 (t, 2H, NH), 7.09, 6.95 (2 s, 1:3H, ArH), 5.79 (d, 4H, *J* = 7.1 Hz, outer OCH_2O), 4.73 [t, 4H, *J* = 8.1 Hz, $CH(CH_2)_4$], 4.36 (d, 4H, inner OCH_2O), 4.26 (d, 4H, *J* = 4.9 Hz, $ArCH_2NH$), 3.23 [d, 4H, *J* = 12.5 Hz, $C(O)CH_2P(O)$], 2.35–2.1 (m, 8H, $CHCH_2$), 1.97 (s, 6H, $ArCH_3$), 1.5–1.15 [m, 24H, $CHCH_2(CH_2)_3$], 0.91 (t, 12H, *J* = 6.7 Hz, CH_3). – ^{13}C NMR: δ = 164.3, 164.2 [s, NC(O)], 153.7 (s, $ArCOCH_2O$), 138.4, 137.5 (s, ArCCH), 132.5–128.8 (P-phenyl), 124.1 (s, $ArCCH_3$), 123.0 (s, $ArCCH_2$), 120.3, 117.0 (d, ArCH), 99.2 (t, OCH_2O), 38.7 [dt, *J* = 225 Hz, $C(O)CH_2P(O)$], 37.0 (d, ArCHAr), 34.4 (t, $ArCH_2NH$), 10.4 (q, $ArCH_3$). – $C_{84}H_{96}N_2O_{12}P_2 \cdot 0.5\ CH_2Cl_2$ (1435.1): calcd. C 70.12, H 6.72, N 1.94; found C 70.18, H 7.09, N 2.05.

1,2-Bis(diphenyl-N-methylcarbamoylmethylphosphane oxide)-3,4-dimethylcavitand (**11c**) was prepared by the reaction of the 1,2-bis(aminomethyl)-3,4-dimethylcavitand **9c** (248 mg, 0.28 mmol) and *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**) (0.47 g, 0.91 mmol) in toluene (25 ml) for 11 h. Yield 342 mg (90%), m.p. 132–133°C (CH_2Cl_2/MeOH). – MS, *m/z* (%): 1409.7 (100) [M^+ + Na]. – ^{1}H NMR: δ = 7.72–7.64 and 7.53–7.42 (2 m, 8:12H, phenyl), 7.17 (t, *J* = 5.1 Hz, 2H, NH), 7.09, 6.96 (2 s, 2:2H, ArH), 5.86, 5.78, 5.70 (3 d, 1:2:1H, *J* = 7.2 Hz, outer OCH_2O), 4.75, 4.72, 4.69 [3 t, 1:2:1H, *J* = 7.0 Hz, $CH(CH_2)_4$], 4.40–4.22 (m, 4H, inner OCH_2O, 4H, $ArCH_2NH$), 3.24 [d, 6H, *J* = 12.7 Hz, $C(O)CH_2P(O)$], 2.25–2.05 (m, 8H, $CHCH_2$), 1.97 (s, 6H, $ArCH_3$), 1.45–1.15 [m, 24H, $CHCH_2(CH_2)_3$], 0.92 (t, 12H, *J* = 6.9 Hz, CH_3). – ^{13}C NMR: δ = 164.3 [s, NC(O)], 153.9, 153.7, 153.5, 153.3 (s, $ArCOCH_2O$), 138.6, 138.0, 137.9, 137.4 (s, ArCCH), 132.5–128.8 (P-phenyl), 123.9 (s, $ArCCH_3$), 122.9 (s, $ArCCH_2$), 120.2, 117.1 (d, ArCH), 99.9, 99.2 (t, OCH_2O), 39.0 [dt, *J* = 259 Hz, $C(O)CH_2P(O)$], 37.0 (d, ArCHAr), 34.5 (t, $ArCH_2NH$), 10.5 (q, $ArCH_3$). – $C_{84}H_{96}N_2O_{12}P_2 \cdot H_2O$ (1405.6): calcd. 71.78, H 7.03, N 1.99; found C 71.72, H 7.00, N 2.00.

Tris(diphenyl-N-methylcarbamoylmethylphosphine oxide)methylcavitand (**11d**) was prepared by the reaction of the tris(aminomethyl)methylcavitand **9d** (206 mg, 224 μmol) and *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**) (0.39 g, 0.74 mmol) in toluene (20 ml) for 6 h. Yield 316 mg (86%), m.p. 126–128°C (CH_2Cl_2/MeOH). – MS, *m/z* (%): 1668.2 (100) [M^+ + Na]. – ^{1}H NMR: δ = 7.72–7.64 and 7.49–7.35 (2 m, 12:18H, phenyl), 7.19 (t, 3H, NH), 7.07, 6.94 (2 s, 3:1H, ArH), 5.79, 5.72 (2 d, 2:2H, *J* = 7.1 Hz, outer OCH_2O), 4.71, 4.68 [2 t, 2:2H, *J* = 7.7 Hz, $CH(CH_2)_4$], 4.35, 4.29 (2 d, 2:2H, *J* = 7.5 Hz, inner OCH_2O), 4.23 (d, 6H, *J* = 4.9 Hz, $ArCH_2NH$), 3.25 [d, 6H, *J* = 12.8 Hz, $C(O)CH_2P(O)$], 2.3–2.05 (m, 8H, $CHCH_2$), 1.96 (s, 3H, $ArCH_3$), 1.5–1.15 (m, 24H, $CHCH_2(CH_2)_3$], 0.92 (t, 12H, *J* = 6.9 Hz, CH_3). – ^{13}C NMR: δ = 164.3, 164.2 [s, NC(O)], 153.9, 153.8, 153.6, 153.5 (s, $ArCOCH_2O$), 138.6, 138.1, 137.9, 137.5 (s, ArCCH), 132.4–128.8 (P-phenyl), 124.2 (s, $ArCCH_3$), 123.2 (s, $ArCCH_2$), 120.0, 116.9 (d, ArCH), 99.8, 99.2 (t, OCH_2O), 39.3 [dt, *J* = 243 Hz, $C(O)CH_2P(O)$], 36.9 (d, ArCHAr), 34.3 (t, $ArCH_2NH$), 10.5 (q, $ArCH_3$). – $C_{98}H_{108}N_3O_{14}P_3 \cdot H_2O$ (1662.9): calcd. C 70.79, H 6.67, N 2.53; found C 70.55, H 6.87, N 2.26.

Extraction Experiments

Solutions: The 10^{-4} M salt stock solutions were prepared by dissolving the required amounts of the appropriate metal nitrate or chloride salt $M^{n+}(X^-)_n$ and LiPic in 10^{-3} M HNO_3 and adjusting the total volume of the solution to 20 ml using volumetric glassware. The pH of the solutions was close to pH 3.0, and adjusted to pH 3.0 by adding small amounts of LiOH or 0.1 M HNO_3 if necessary. The metal picrates were prepared in situ in the stock solutions resulting from the presence of an excess (10^{-2} M) lithium picrate in the 10^{-4} M salt solutions. The salt solutions were spiked with the appropriate radiotracer (^{22}Na, ^{90}Sr, ^{137}Cs, ^{152}Eu or $^{235,238}UO_2$) by adding a small amount (20–200 μl) of a radiotracer solution to the respective salt solutions. The spiked Fe^{III} stock solution was prepared by dissolving the required amounts of $FeCl_3$ and LiPic in 2 ml of 0.1 M HCl ^{59}Fe-tracer solution and adjusting the volume to 20 ml with H_2O, followed by pH correction to pH 3.0 by adding LiOH giving a deviated solution of 10^{-3} M HCl and $0.9 \cdot 10^{-2}$ M LiCl. The 10^{-3} M stock solutions of the ligands were prepared by dissolving the appropriate amount of the ligands in 20 ml of CH_2Cl_2.

Procedures: Equal volumes (1.0 ml) of the organic and the aqueous solutions were pipetted in a glass stoppered glass tube and magnetically stirred at ambient temperatures (22–24°C) for at least 20 min (60 min for Fe^{III} extraction experiments)[16] to ensure complete equilibration. The solutions were disengaged by centrifugation (1600 rpm for 10 min) and equal aliquots (0.5 ml) of the organic and aqueous phases were pipetted out. The gamma-activity in both samples was determined with a LKB Wallac Compu-Gamma NaI(Tl) scintillation counter, except for the uranium experiments where liquid scintillation counting was used. The percentage of the cation extracted in the organic phase (%E = E · 100%), defined as the ratio of the activity in the organic phase (A_0) and the total activity in both the organic and the aqueous phase (A_a), is expressed by eq. 1:

$$\%E = \left(\frac{A_0}{A_a + A_0}\right) \cdot 100\% \qquad (1)$$

Variation of ligand concentration experiments were performed by taking suitable aliquots of the stock solution and adjusting the volume to 1.0 ml by adding CH_2Cl_2. The solutions were not pre-equilibrated with the aqueous phase, as the partitioning of the species (e.g. HNO_3, LiPic, or $LiNO_3$) to the organic phase due to the low salt concentrations in the aqueous phase can be neglected. Due to the mutual solubilities of CH_2Cl_2 and water[17], slight extraction ($\%E_{Eu} < 0.4$) was observed in control experiments. The reported extraction percentages are the average of at least four (metal extraction) or two (concentration variation) experiments. The error in the reported extraction percentages is <2%E (<4%E for Sr^{II} and Fe^{III}). The errors in the K_{ex} values are less than 5%.

Determination of Extraction Coefficients (K_{ex}): The extraction of metal cations (M^{n+}) accompanied by n anions and a neutral organic ligand (L) can be described by the general expression given in eq. 2,

$$[M^{n+}]_w + n \cdot [X^-]_w + [L]_o \rightleftarrows [M \cdot X_n \cdot L]_o \qquad (2)$$

where $M = Eu^{3+}$, X = picrate, $n = 3$, and the subscripts o and w denote the presence of the species in the organic or aqueous phase. The assumptions are made that the partition of the ligand to the aqueous phase is negligible ($[L]_w \approx 0$). The presence in the organic phase of $M(Pic)_3$ and $M \cdot X'_3 \cdot L$ species (with $X' = NO_3^-$ or Cl^-; the initial anions of the salts) and the extraction of mixed complexes ($M \cdot X_n \cdot X'_{(3-n)} \cdot L$) is also negligible, as was confirmed by control experiments. The extraction coefficient for the 1:1 complexation K_{ex} is then described by eq. 3:

$$K_{ex} = \frac{[Eu \cdot Pic_3 \cdot L]_o}{[Eu^{3+}]_w \cdot [Pic^-]_w^3 \cdot [L]_o} \qquad (3)$$

As the extraction coefficients (K_{ex}) cannot be determined from log D vs. log $[L]_o$ plots[2], the K_{ex} values for the 1:1 complexes have been calculated from eq. 3 applying the method developed by Cram et al.[18] Assuming that, when (i) $[L]_{o,i} = [Eu^{3+}]_{w,i} = 10^{-4}$ M, the cation is extracted in a 1:1 stoichiometry, and (ii) the variation in the aqueous picrate concentration, $[Pic^-]_w$, is negligible as $[Pic^-]_w \approx [Pic^-]_{w,i} = 10^{-2}$ M, the extraction coefficients for the 1:1 complexes K_{ex} are expressed by eq. 4:

$$K_{ex} = \frac{E}{([Eu^{3+}]_{w,i} - E \cdot [L]_{o,i}) \cdot ([Pic^-]_{w,i})^3 \cdot (1 - E)} \qquad (4)$$

The distribution coefficient D is defined by the general expression in eq. 5 as the ratio of the metal concentration in the organic and in the aqueous phase:

$$D_M = \frac{\Sigma (M)_o}{\Sigma (M)_w} = \frac{E}{1 - E} \qquad (5)$$

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