Novel Resorcinarene Cavitand-Based CMP(O) Cation Ligands: Synthesis and Extraction Properties

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Tetrafunctionalized resorcinarene cavitands (**4**−**6**) have been synthesized starting from tetrakis(bromomethyl)cavitand **3**. New cavitand-based cation ligands with (carbamoylmethyl)phosphonate (CMP) and -phosphine oxide (CMPO) moieties (**8a**,**b** and **9a**,**b**) were prepared via two different routes in good (45−86%) overall yields. The ligands (**8a**,**b** and **9b**) are very effective europium extractants. Ph_2CMPON(Pr)-cavitand **8b** has the highest extraction constant, determined with radiotracer experiments, for 1:1 complexation with Eu(picrate)$_3$ ($K_{ex}^1 = 2.7 \times 10^{12}$ M^{-4}). The steric preorganization of the four CMP(O) moieties on the resorcinarene cavitand improves the efficiency and selectivity [of Eu(III) over UO_2(II) and Fe(III)] of the metal extraction processes, compared to simple CMP(O) extractants.

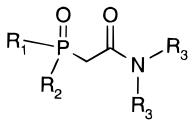
Introduction

Treatment of burned fuel from nuclear power generation is necessary to allow differentation of the radioactive wastes and their subsequent handling, treatment, and storage. In the reprocessing step at the back-end of the nuclear fuel cycle, uranium and plutonium can be quantitatively recovered in the PUREX (*p*lutonium *ur*anium *ex*traction) process.[1] The long term radiotoxicity (and heat production) of the high-level liquid waste (HLLW) generated in the PUREX process is mainly due to the transplutonium elements americium and curium.

The most commonly used process for the recovery of these highly radiotoxic trivalent trans-plutonium actinides, the TRUEX (*tr*ans*u*ranium *ex*traction) process,[2] utilizes (carbamoylmethyl)phosphoryl [CMP(O)] derivatives as organic extractants (the general structure of the CMP(O) derivatives is depicted in Chart 1). The influence of the phosphorus moiety (phosphonate or phosphinate vs phosphine oxide), of the phosphorus substituents (alkyl vs aryl), and of the length of the spacer [methylene vs ethylene; CMP(O) vs CEP(O)] on the extraction properties of these ligands under various conditions has extensively been studied.[3,4]

Generally, in the TRUEX process the trivalent actinides and lanthanides (fission products which are about 50 times more abundant in the HLLW) are extracted as complexes with two to four CMP(O) molecules, depending on the conditions.[4] Preorganization of the complexing CMP(O) groups will favor the strengths of complexation as the coordinating moieties are already grouped and positioned. Recently, Böhmer et al.[5] showed that macrocyclic molecules are suitable platforms for ligands with preorganized ligating sites, e.g. calix[4]arenes with four CMPO moieties. Compared with the simple *N*,*N*-diisobutyloctylphenyl-CMPO the same extraction efficiencies were reached at 250 times lower extractant concentrations.

Chart 1. General Structure of the CMP(O) Derivatives



$R_1 = R_2$ = O-alkyl — carbamoylmethylphosphonate (CMP)
R_1 = O-alkyl; R_2 = aryl, alkyl — carbamoylmethylphosphinate (CMP)
$R_1 = R_2$ = aryl, alkyl — carbamoylmethylphosphine oxide (CMPO)

Ligands based on functionalized resorcinarenes should allow a high degree of preorganization of the complexing moieties due to the rigidity of the cavitand frame. So far resorcinarene cavitands[6] have mainly been used for the synthesis of carcerands and carceplexes.[7] However, to the best of our knowledge its rigid molecular platform has not yet been exploited for the design of specific receptor molecules.[8,9] The limited availability of cav-

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(1) (a) McKay, H. A. C.; Miles, J. H.; Swanson, J. L. *Science and Technology of Tributyl Phosphate*; Schulz, W. W., Navratil, J. D., Eds.; CRC Press: Boca Raton, 1984; p 1. (b) Miles, J. H. *Science and Technology of Tributyl Phosphate*; Schulz, W. W., Navratil, J. D., Eds.; CRC Press: Boca Raton, 1984; p 11.

(2) For example, see: (a) Horwitz, E. P.; Kalina, D. G.; Diamond, H.; Vandegrift, G. F. *Solv. Extr. Ion Exch.* **1985**, *3*, 75. (b) Horwitz, E. P.; Schulz, W. W. *New Separation Chemistry, Techniques for Radioactive Waste and other Specific Applications*; Horwitz, E. P., Schulz, W. W., Eds.; Elsevier Applied Science: New York, 1991; p 21.

(3) (a) Siddall, III, T. H. *J. Inorg. Nucl. Chem.* **1963**, *25*, 883. (b) Siddall, III, T. H. *J. Inorg. Nucl. Chem.* **1964**, *26*, 1991.

(4) For some examples see: (a) Kalina, D. G.; Horwitz, E. P.; Kaplan, L.; Muscatello, A. C. *Sep. Sci. Technol.* **1981**, *16*, 1127. (b) Horwitz, E. P.; Kalina, D. G.; Kaplan, L.; Mason, G. W. *Sep. Sci. Technol.* **1982**, *17*, 1261. (c) Myasoedov, B. F.; Chmutova, M. K.; Kochetkova, N. E.; Koiro, O. E.; Pribylova, G. A.; Nesterova, N. P.; Medved, T. Ya.; Kabachnik, M. I. *Solv. Extr. Ion Exch.* **1986**, *4*, 61. (d) Horwitz, E. P.; Martin, K. A.; Diamond, H.; Kaplan, L. *Solv. Extr. Ion Exch.* **1986**, *4*, 449. (e) Horwitz, E. P.; Dietz, M. L.; Fisher, D. E. *Solv. Extr. Ion Exch.* **1991**, *9*, 1.

(5) Arnaud-Neu, F.; Böhmer, V.; Dozol, J.-F.; Grüttner, G.; Jakobi, R. A.; Kraft, D.; Mauprivez, O.; Rouquette, H.; Schwing-Weill, M.-J.; Simon, N.; Vogt, W. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1175.

(6) Throughout this paper the trivial name *cavitand* will be used for the rigidified tetrameric resorcinarene frame. The official IUPAC name for the tetrakis(XX)cavitand is 7,11,15,28-tetrakis(XX)-1,21,23,25-tetrapentyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin, in which the XX refers to the substituents.

(7) For reviews, see: (a) Cram, D. J.; Cram, J. M. *Container Molecules and their Guests, Monographs in Supramolecular Chemistry;* Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, 1994; Vol. 4. (b) Timmerman, P.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron* **1996**, 52, 2663.

(8) Cavitands have been used in combination with calixarenes for complexation of steroids: Higler, I.; Timmerman, P.; Verboom, W.; Reinhoudt, D. N. *J. Org. Chem.* **1996**, *61*, 5920.

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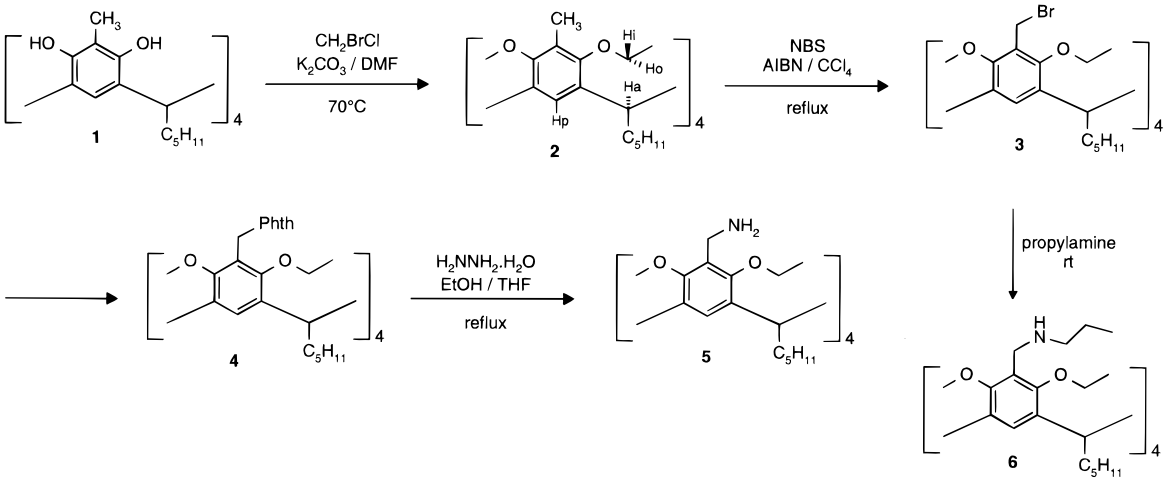
Scheme 1. Synthesis of the Aminomethylcavitands



itands which are suitable for a wide range of further functionalizations may account for this.[10] Attachment of ligating sites to the rigid cavitand frame allows in principle a tight preorganization of the coordinating sites. Furthermore, the limited flexibility of the ligating sites is favorable in cases where the coordinating atoms of the ligand have to compete with solvent molecules or anions.[11]

In this paper we present the synthesis and the first europium (selected as representative for the trivalent actinides americium and curium)[12] extraction results of a new type of resorcinarene cavitand-based ligand functionalized with (carbamoylmethyl)phosphonate and -phosphine oxide groups.

Results and Discussion

Synthesis. The CMP(O)-based cavitands have been prepared starting from the alkyl(aminomethyl)cavitands **5** and **6**, the synthesis of which is summarized in Scheme 1. Reaction of the known tetramethyloctol **1**[13] with 17 equiv of CH_2BrCl in DMF and K_2CO_3 as a base afforded bridging of the neighboring hydroxyl groups, rigidifying the molecule to give tetramethylcavitand **2** in 92% yield.[14] The structure of the product followed from the characteristic cavitand ^{1}H NMR signals: one singlet (at 6.97 ppm) for the aromatic hydrogen (H_p) and doublets (at 5.87 and 4.25 ppm) for the outer (H_o) and inner bridge hydrogens (H_i), respectively. The bridging reaction proceeds faster, in higher yield, and in the presence of fewer equivalents of CH_2BrCl, compared to the reaction of the corresponding tetrabromooctols.[15] This might be attributed to the activating influence toward alkylation of the electron-releasing methyl group on the aromatic ring ortho to the hydroxyl groups.

Bromination[16,17] of methylcavitand **2** with NBS in CCl_4 with AIBN as the catalyst gave tetrakis(bromomethyl)-cavitand **3** in 93% yield after recrystallization.[18] In the ^{1}H NMR spectrum the aromatic hydrogen shifted upfield to 7.13 ppm and the doublets of the hydrogens of the methyleneoxy bridges shifted to 6.02 and 4.77 ppm, respectively, due to the introduction of a bromo atom at the methyl groups.

Tetrakis(aminomethyl)cavitand **5** was synthesized in two steps from (bromomethyl)cavitand **3**. Reaction of **3** with potassium phthalimide and tributylhexadecylphosphonium bromide as phase-transfer catalyst in refluxing toluene[19] gave tetrakis(phthalimidomethyl)cavitand **4** in 72% yield. The phthalimido groups of **4** were removed by treatment with hydrazine hydrate in refluxing ethanol/THF, to give tetrakis(aminomethyl)cavitand **5** in 94% yield.

Tetrakis(propylaminomethyl)cavitand **6** was synthesized directly from (bromomethyl)cavitand **3**, by dissolving **3** in *n*-propylamine at room temperature. In this almost instantaneous reaction propylamine is reagent, as well as both solvent and base. The reaction proceeds in nearly quantitative yield and no overalkylation of the amino functions was observed according to the ^{1}H NMR and mass (FAB) spectra.

CMP(O)-Based Ligands. The synthesis of (carbamoylmethyl)phosphonate, -phosphinate, and -phosphine oxide derivatives has been extensively studied by Horwitz et al.[20] In our study the CMP(O) ligating sites are introduced via a two-step route starting from the amino

(9) Some examples of metal ligands based on (non-cavitand) resorcinarene derivatives have been described. (a) Octols with eight acetyl esters or amides: Fransen, J. R.; Dutton, P. J. *Can. J. Chem.* **1995**, *73*, 2217. (b) Monoanionic form of tribridged−diol resorcinarenes: Sorrell, T. N.; Pigge, F. C.; White, P. S. *Inorg. Chem.* **1994**, *33*, 632. (c) Potential ligands for silver and copper(II): Egberink, R. J. M.; Cobben, P. L. H. M.; Verboom, W.; Harkema, S.; Reinhoudt, D. N. *J. Incl. Phenom.* **1992**, *12*, 151.

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(11) Boerrigter, H.; Konings, R. J. M.; Cordfunke, E. H. P.; Verboom, W.; Reinhoudt, D. N. *GLOBAL'*95, International Conference on Evaluation of Emerging Nuclear Fuel Cycle Systems; 1995, Vol. 2, p 1252.

(12) (a) Seaborg, G. T. *Radiochim. Acta* **1993**, *61*, 115. (b) Choppin, G. R.; Rizkalla, E. N. *Handbook of the Physics and Chemistry of Rare Earths;* Gschneider, K. A., Jr., Eyring, L., Choppin, G. R., Lander, G. H., Eds.; Elsevier Science: Amsterdam, 1994; Vol. 18, p 559.

(13) Tunstad, L. M.; Tucker, J. A.; Dalcanale, E.; Weiser, J.; Bryant, J. A.; Sherman, J. C.; Helgeson, R. C.; Knobler, C. B.; Cram, D. J. *J. Org. Chem.* **1989**, *54*, 1305.

(14) Although the crude product after workup appeared to be pure based on the ^{1}H NMR spectrum, some impurities were present that interfered with subsequent reactions. After chromatography of the crude product over 2 cm of silica, cavitand **2** was obtained in pure form.

(15) (a) H. Boerrigter, Unpublished results. (b) Timmerman, P.; Boerrigter, H.; Verboom, W.; Van Hummel, G. J.; Harkema, S.; Reinhoudt, D. N. *J. Incl. Phenom.* **1994**, *19*, 167. (c) Bryant, J. A.; Blanda, M. T.; Vicenti, M.; Cram, D. J. *J. Am. Chem. Soc.* **1991**, *113*, 2167. (d) Cram, D. J.; Karbach, S.; Kim, H.-E.; Knobler, C. B.; Maverick, E. F.; Ericson, J. L.; Helgeson, R. C. *J. Am. Chem. Soc.* **1988**, *110*, 2229.

(16) Sorrell, T. N.; Pigge, F. C. *J. Org. Chem.* **1993**, *58*, 784.

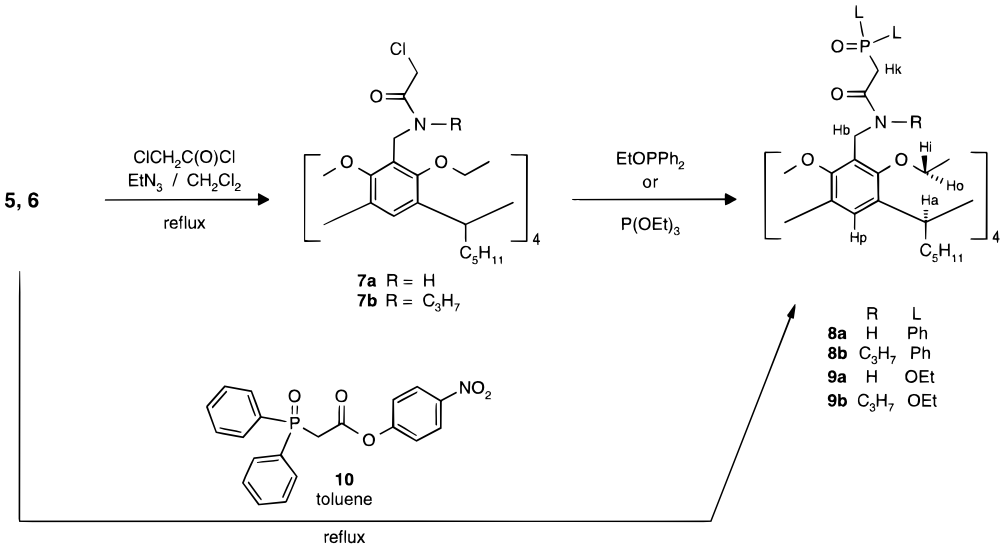
(17) The conditions reported by Sorrell and Pigge were (in our hands) not successful.

(18) Boerrigter, H.; Verboom, W.; Van Hummel, G. J.; Harkema, S.; Reinhoudt, D. N. *Tetrahedron Lett.* **1996**, *37*, 5167.

(19) Landini, D.; Rolla, F. *Synthesis* **1976**, 389.

(20) Gatrone, R. C.; Kaplan, L.; Horwitz, E. P. *Solv. Extr. Ion Exch.* **1987**, *5*, 1075.

Scheme 2. Synthesis of the Tetrasubstituted Ligands



compounds **5** or **6**, viz. acylation of the amines with chloroacetyl chloride, followed by an Arbusov[21] reaction on the carbon atom with the β-halogen atom. Acylation of (aminomethyl)- and [(propylamino)methyl]cavitands **5** and **6** with chloroacetyl chloride and Et_3N as a base in CH_2Cl_2 afforded tetrakis[(chloroacetamido)methyl]cavitand **7a** in 93% yield and tetrakis[(*N*-propylchloroacetamido)-methyl]cavitand **7b** in 90% yield, respectively (Scheme 2).

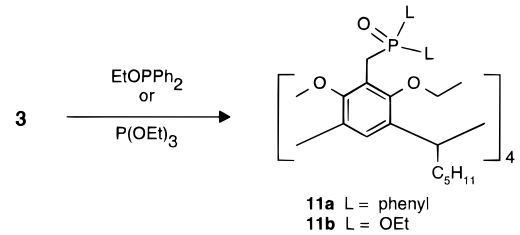
Arbusov reaction of cavitand **7a** with ethyl diphenylphosphinite gave tetrakis[diphenyl[(*N*-methylcarbamoyl)methyl]phosphine oxide]cavitand (Ph_2CMPO−N(H)-cavitand) **8a** in 78% yield. In the case of cavitand **7b,** the corresponding tetrakis[diphenyl[(*N*-methyl-*N*-propylcarbamoyl)methyl]phosphine oxide]cavitand (Ph_2-CMPO−N(Pr)-cavitand) **8b** was obtained in 80% yield. Arbusov reaction of cavitands **7a**,**b** with triethyl phosphite afforded the [(carbamoylmethyl)phosphonate]cavitands ($(EtO)_2$CMP−N(H)- and $(EtO)_2$CMP−N(Pr)-cavitands) **9a**,**b** in 57% and 93% yield, respectively.[22]

Recently, Böhmer et al.[5] reported the preparation of calix[4]arene-based ligands containing four diphenyl-(carbamoylmethyl)phosphine oxide [Ph_2CMPO−N(H)] moieties. However, they were not successful in introducing the phosphoryl function via the Arbusov route.[5] In their approach an activated CMPO-function, *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**), prepared via a three-step synthesis,[5] was directly attached via aminolysis to tetraaminocalix[4]arenes. Following this approach, with optimized reaction conditions, [diphenyl(carbamoylmethyl)phosphine oxide]cavitands **8a**,**b** were also synthesized from (aminomethyl)- and [(propylamino)-methyl]cavitands **5** and **6** in 98% and 94% yield, respectively. Although this is a simple synthesis, it is less suitable for the synthesis of compounds with substituents other than phenyl at phosphorus (compare compounds **8** vs **9**).

(21) For a review see: Bhattacharya, A. K.; Thyagarajan, G. *Chem. Rev. (Washington, D.C.)* **1981**, *81*, 415.

(22) In general, the purification of reaction products from Arbusov reactions is difficult, due to the high boiling points of the Arbusov reagents and the instability of the products on different column materials (e.g. silica and aluminum oxide). Recrystallization or precipitation of the products are useful in some cases, but does often not allow satisfying results. Purification with Sephadex LH-20 column chromatography is an excellent method in these cases, as the Arbusov reagents are generally much smaller (have a smaller molecular volume) than the macrocyclic derivatives. Furthermore, no product is lost due to decomposition on, or interactions with, the column material.

Scheme 3. Synthesis of the Phosphorylmethyl Cavitands



The ^{1}H NMR spectrum of Ph_2CMPO−N(H)-cavitand **8a** exhibits characteristic signals for the aromatic cavitand hydrogen (at 7.06 ppm), the doublets for the outer and inner bridge hydrogens (at 5.55 and 4.43 ppm) and the doublet for the CMPO methylene hydrogens (H_k) at 3.24 ppm with a phosphorus coupling constant ($^2J_{PH}$) of 13.7 Hz. The ^{1}H NMR signals for the corresponding $(EtO)_2$CMP−N(H)-cavitand **9a** were found at 7.14 (H_p), 5.95 and 4.18 (H_o and H_i), and 2.90 ppm with $^2J_{PH} = 21.1$ Hz for H_k.

The ^{1}H NMR spectra of the derivatives with the propyl-substituted amide moieties (cavitands **7b**, **8b**, and **9b**) are very complicated and show multiple signals for all hydrogens due to the internal hindered rotation around the amide N−C(O) bonds. In particular it is very pronounced for the absorption of the aromatic (H_k) and the methyleneoxy bridge hydrogens (H_o and H_i). The multiple signals of **7b**, **8b**, and **9b** (partly) coalesced to one (broad) signal when the spectra were recorded at elevated temperatures (408 K) in $C_2D_2Cl_4$.

Phosphorylmethyl Cavitands. For reasons of comparison with the CMP(O)-derivatized cavitands **8** and **9**, two ligands were included in our study containing phosphoryl moieties without the amide function. Tetrakis(diphenylmethylphosphine oxide)cavitand (Ph_2P(O)-cavitand) **11a** was prepared in an Arbusov reaction of (bromomethyl)cavitand **3** with ethyl diphenylphosphinite in 78% yield. Similary, the reaction of **3** with triethyl phosphite afforded tetrakis(diethyl methylphosphonate)-cavitand ($(EtO)_2$P(O)-cavitand) **11b** in 94% yield (Scheme 3).

Similar to ligands **8a** and **9a**, the structure of Ph_2P-(O)-cavitand **11a** followed from the ^{1}H NMR signals for the aromatic cavitand hydrogen (at 6.81 ppm), the doublets for the outer and inner bridge hydrogens (at 5.23

Table 1. Extraction of Cations with Tetrafunctionalized Cavitands

	percentage of cation extracted, %E[a]					
	8a	**8b**	**9a**	**9b**	**11a**	**11b**
Na^+	<1	<1	<1	<1	<1	<1
Cs^+	<1	<1	<1	<1	<1	<1
Sr^{2+}	80	94	89	67	64	93
UO_2^{2+}	92	98	54	97	82	25
Fe^{3+} [b]	55	90	83	66	24	51
Eu^{3+}	93	97	49	99	75	10

[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] $[L]_{o,i} = 10^{-3}$ M; $[Fe^{3+}]_{w,i} = 10^{-4}$ M; $[LiPic]_w = 10^{-2}$ M; $[LiCl]_w = 0.9 \times 10^{-2}$ M; $[HCl]_w = 10^{-3}$ M; pH = 3.0.

and 4.39 ppm, respectively), and the doublet for the methylene hydrogens at 3.46 ppm with a phosphorus coupling constant ($^2J_{PH}$) of 14.7 Hz. The ^{1}H NMR signals for the corresponding $(EtO)_2P(O)$-cavitand **11b** are present at 6.99 (H_p), 5.81 and 4.69 (H_o and H_i), and 2.94 ppm with $^2J_{PH} = 22.5$ Hz (H_k methylene hydrogens).

Extraction. To study the influence of different phosphorus and amide substituents, picrate (2,4,6-trinitrophenolate) extractions were carried out with the new ligands.[23] Picrate is known to form preferentially second sphere complexes and, in addition, the partitioning of the anions from the aqueous to the organic phase will not be extraction limiting due to its lipophilicity.[24] In the extraction studies europium was selected as a general representative for the trivalent actinides (e.g. americium and curium) and lanthanide group elements.[12] The selectivity for europium over five other elements was also studied, viz. sodium, iron [Fe(III)],[4b] strontium, cesium,[25] and uranium [as UO_2(II)].[1] These elements were selected both for their presence in the nuclear waste, as well as for the variation in charge and physical properties of the cations.

Metal Extractions. The results of the extraction experiments with the new phosphoryl ligands **8**, **9**, and **11** are summarized in Table 1 (the extraction properties are expressed as %E, the percentage cation extracted; see the Experimental Section).

All phosphoryl ligands exhibit high extraction values for the elements Sr(II), UO_2(II), Fe(III), and Eu(III). Furthermore, none of the ligands showed any significant affinity for the first row transition metals Na(I) and Cs(I) (with $\%E_{Na,Cs} < 1\%$, in the range of the blank extraction). The highest extraction values for both Eu(III) and UO_2(II), which are extracted essentially to the same extent, were found with the CMP(O) ligands **8a**,**b** and **9b**. Although ligand **11b** hardly extracts Eu(III) and UO_2(II), **11b** might be applied as a strontium selective extractant, as the extraction of Sr(II) is quite remarkable. The %E of **11a** for Eu(III) and UO_2(II) is higher than for **11b**, due to the increased basicity of the phosphoryl oxygens of **11a**.

The %E values of the extractable cations have been calculated as distribution coefficients (D), and their separation factors (S) compared to Eu(III) are given in Table 2.[26] Comparison of the $S_{Eu/M}$ values reveals no clear relation between structural properties of the ligands and physical properties of the metal cations employed. Under the experimental conditions ligand **9b** is the most efficient and selective extractant for Eu(III). Also **8a** and **8b** are efficient Eu(III) extractants, but less selective over Sr(II) and Fe(III).

Table 2. Distribution Coefficients and Separation Factors

	distribution coefficients[a]				separation factors[b]		
	D_{Sr}	D_{UO_2}	D_{Fe}	D_{Eu}	$S_{Eu/Sr}$	S_{Eu/UO_2}	$S_{Eu/Fe}$
8a	4.0	11.5	1.2	14.1	3.5	1.2	12
8b	15.7	49.0	9.0	28.2	1.8	0.58	3.1
9a	8.1	1.2	4.9	0.97	0.12	0.82	0.20
9b	1.7	32.3	1.9	97.7	55	3.0	50
11a	1.8	4.5	0.32	3.0	1.7	0.65	9.3
11b	13.3	0.33	1.0	0.11	0.01	0.33	0.11

[a] $D = \sum(M)_o/\sum(M)_w = E/(1 - E)$. [b] $S_{a/b} = D_a/D_b$.

Comparison of the Cavitand Ligands with CMP(O). The ligands **8a**,**b** and **9b** have high distribution ratios for U, but Eu (which is comparable with Am)[12] is preferentially extracted (see Table 2). The simple CMP(O) derivatives, on the other hand, have initially been developed to separate Pu and U, and the distribution ratios for U are generally much higher than for Am.[2b,27,28] The selectivities of the extraction of Eu over Fe(III) are also improved with the cavitand ligands **8a**,**b** and **9b**, e.g. the separation factors are $S_{Eu/M} \geq 1$ (M = U, Fe). However, with simple CMP(O) derivatives the extraction selectivity of Am over Fe is reversed (Fe is preferentially extracted at low acidity $[HNO_3] \sim 10^{-2}$ M).[4a] The ligands **8** and **9** do not extract Na and Cs, but Sr is significantly extracted, while Sr,[2a,4e,29] as well as Na and Cs,[30] are not extracted by any of the simple CMP(O) ligands ($D < 10^{-2}$), independent of the nitric acid concentration.

Due to the different experimental conditions, comparison of our results with those obtained with related CMPO-functionalized macrocyclic ligands (tetra-CMPO calix[4]arene derivatives) reported by Böhmer et al.[5] is not possible. However, the trends in the extraction behavior are similar, and both resorcinarene- and calix[4]arene-based ligands are much more efficient than the simple CMP(O) derivatives.

Extraction Constants. In general the stoichiometry of the extracted complexes and the extraction constants (K_{ex}) can be determined from log D vs log [L] plots (see Experimental Section). Therefore, the dependence of the extraction of Eu(III) on the concentration of the ligands was studied. The data are presented in Figure 1 as plots of log D_{Eu} vs log $[L]_{o,i}$, the initial ligand concentration, because the values of the ligand equilibrium concentrations ($[L]_o$) are unknown.[31] The variations of log D_{Eu} as function of log $[L]_{o,i}$ exhibit a curved trend of which the curvature is more pronounced with increasing strength of the extractant,[32] and the three strongest extractants (**8a**, **9b**, and **8b**) all reach a maximum extraction (distribution).

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(24) Takeda, Y. *Top. Curr. Chem.* **1984**, *121*, 1.

(25) Horwitz, E. P.; Dietz, M. L.; Fisher, D. E. *Solv. Extr. Ion Exch.* **1991**, *9*, 1.

(26) The values presented in Table 2 have been rounded off; however, the calculations were performed with the exact values.

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(31) The value of the equilibrium ligand concentration $[L]_o$ cannot be calculated from the mass balance, as $[L]_{o,i} \sim [Eu^{3+}]_{w,i}$ and thus the assumption $[Eu{\cdot}Pic_3{\cdot}L_p]_o < [L]_o \approx [L]_{o,i}$ cannot be made.

(32) The data points of the extraction of thorium (and to lesser extent europium) with tetra-CMPO calix[4]arene derivatives in the same concentration range in the study of Böhmer et al. can also be interpreted as a curved trend. However, the authors suggested a linear correlation.

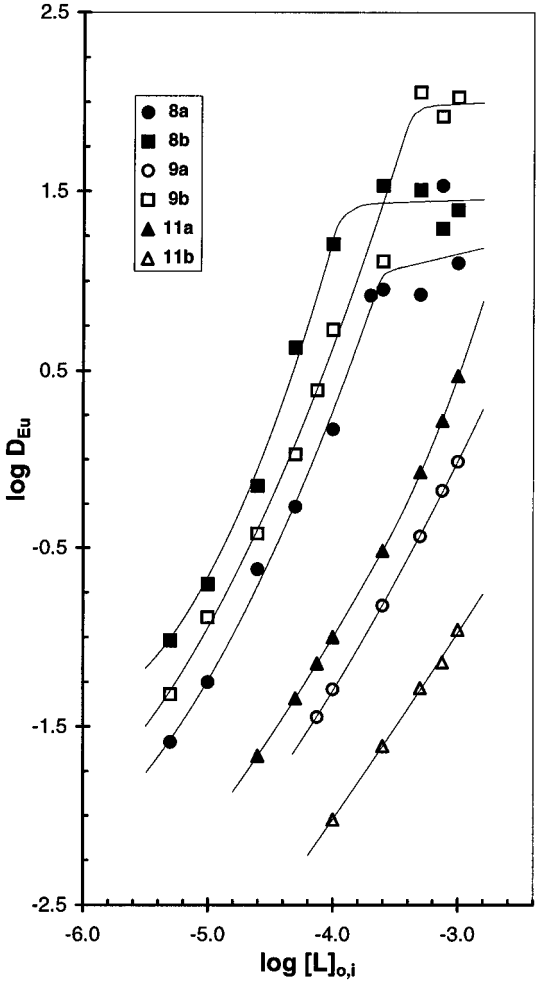

Figure 1. Plots of log D_{Eu} vs log $[L]_{o,i}$; $[Eu^{3+}]_{w,i} = 10^{-4}$ M, $[LiPic]_w = 10^{-2}$ M, $[HNO_3]_w = 10^{-3}$ M; pH = 3.0

In the curved graphs of the ligands **8a**,**b**, **9a**, and **11a,** roughly two regions can be distinguished, (i) excess cation ($[L]_{o,i} < 10^{-4}$ M), and (ii) excess ligand ($[L]_{o,i} > 10^{-4}$ M), that can be attributed to 1:1 and 2:1 stoichiometry of the predominantly extracted species, respectively. In the 1:1 complex both the phosphoryl oxygen and amide carbonyl interact with the cation. The contribution of the amide carbonyl in the complexation is confirmed by IR data, viz. the $\upsilon_{C=O}$ stretching vibrations of the free ligands **8a** (1671 cm^{-1}) and **8b** (1635 cm^{-1}) shift to a lower wavenumber upon complexation with Eu.[33] Unfortunately, the value of the shifts can only be estimated as they shifted under the large 1610 cm^{-1} NO_2 band of the picrate. Approximately, upon complexation the shifts of **8a** and **8b** are 60 and 25 cm^{-1}, respectively, with an estimated error of ± 20 cm^{-1}.[34,35]

On the other hand, in the 2:1 complex, the cation is coordinated mainly by the phosphoryl oxygens, allowing a second molecule to occupy remaining coordination sites. As the phosphoryl oxygens are stronger donating than the amide carbonyls,[4d,36] the cation is preferably enclosed by phosphoryl groups of two ligand molecules.

Table 3. Extraction Constants of 1:1 Complexes

	$E^a \times 10^2$	K_{ex} [M^{-4}]		$E^a \times 10^2$	K_{ex} [M^{-4}]
8a	60	3.7×10^{10}	**9b**	84	3.4×10^{11}
8b	94	2.7×10^{12}	**11a**	9.1	1.1×10^{9}
9a	4.9	5.4×10^{8}	**11b**	0.94	9.6×10^{7}

[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.

For the strongest Eu(III) complexing ligand (**8b**), the extraction in the concentration range of $[L]_{o,i} < 5 \times 10^{-5}$ M is higher than would be possible in the case when only the presence of 1:1 complexes is assumed, which indicates the formation of 1:2 complexes. Sterically this can be made plausibly when twice two proximal CMPO groups on a ligand coordinate with a cation.

As the K_{ex} values cannot be determined from log D vs log [L] plots, the extraction coefficients for the 1:1 complexes (K_{ex}^1) (summarized in Table 3) have been calculated from eq 1.

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

Equation 1 follows from the general relation for K_{ex}^1, described by eq 4 (see Experimental Section), applying the method developed by Cram et al.,[37] under the assumptions that, in the case of $[L]_{o,i} = [Eu^{3+}]_{w,i} = 10^{-4}$ M, the cation is extracted in a 1:1 stoichiometry and that the variation in the aqueous picrate concentration, $[Pic^-]_w$, is negligible as $[Pic^-]_w \approx [Pic^-]_{w,i} = 10^{-2}$ M.

From Table 3 it follows that the ligands with an amide function, the CMP(O) derivatives **8** and **9**, are stronger extractants than the phosphoryl cavitands **11** (with the exception of **9a**). This can be attributed to a combination of additional complexation of the amide carbonyl and a better geometrical fit of the phosphonate/phosphine oxide due to the longer spacer length.

The presence of a substituent on the amide nitrogen largely influences the extraction; viz. **8b** is a ~75 times stronger extractant than its unsubstituted analogue **8a**, while the K_{ex} value of **9b** is ~650 higher than that of **9a**. The increasing effect on the basicity of the amide carbonyls of **8b** and **9b** due to the introduction of a propyl group cannot solely account for this large difference.[38] Intramolecular "self-complexation" within the CMP(O) moieties of **8a** and **9a** might be an important effect. The phosphine oxide and phosphonate phosphorus oxygens of **8a** and **9a** might coordinate with the amide hydrogen, forming a six-membered ring, which has to adjust its geometry prior to complexation. Both phosphine oxide ligands (**8a** and **8b**) are better europium extractants than their phosphonate analogues (**9a** and **9b**). The difference between **8** and **9** is the result of the stronger basicity of the phosphine oxide oxygen of **8** compared to the phoshinate oxygen of **9**.[4d,36]

(33) A solution in which the ligands were saturated with Eu(III) was prepared by contacting the ligand (2 mL, 10^{-3} M) and europium solutions (2 mL, 10^{-2} M $Eu(NO_3)_3$, 3×10^{-2} M LiPic solution in 10^{-3} M HNO_3) in a standard extraction experiment.

(34) These values are in good agreement with IR data for CMPO derivatives: (a) Martin, K. A.; Horwitz, E. P.; Ferraro, J. R. *Solv. Extr. Ion Exch.* **1986**, *4*, 1149. (b) ref. 4b.

(35) In studies of Am/Eu tracer extractions with simple CMP derivatives under comparable conditions ($[L]_{o,i}$ = 0.08−0.8 M in diisopropylbenzene, $[NH_4SCN]_{w,i} = 10^{-2}$ M, $[HCl]_{w,i} = 10^{-3}$ M, pH 3.0), bidentate behavior was also found. See: Muscatello, A. C.; Horwitz, E. P.; Kalina, D. G.; Kaplan, L. *Sep. Sci. Technol.* **1982**, *17*, 859.

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(38) The protonation data for the secondary and tertiary amides *N*-methylbenzamide and *N*,*N*-dimethylbenzamide: the H_o (half-protonation) values are 2.13 and 1.62, respectively: *The Chemistry of Amides*; Zabicky, J., Patai, S., Eds.; John Wiley & Sons: London, 1970; p 210.

Conclusions

In this paper we present the synthesis of tetrafunctionalized resorcinarene cavitands (**4**, **5**, and **6**) from tetrakis(bromomethyl)cavitand **3**. The CMP(O) ligands **8a**,**b** and **9a**,**b** were prepared via two different routes in good (45−86%) overall yields.

The CMP(O) ligands (**8a**,**b** and **9b**) are very effective europium (which was used as a representative of the lanthanides and trivalent actinides) extractants, because of the steric preorganization of the four CMP(O) moieties on the resorcinarene cavitand. Although uranium is extracted to the same extent as Eu(III) and the selectivity over Fe(III) is small, the selectivities are better than with simple CMP(O) derivatives. Phosphoryl cavitand **11b** extracts Sr(II) very efficiently and is a moderate extractant for the other elements. This illustrates the potential of **11b** as a strontium selective ligand.

Experimental Section

Materials. THF was freshly distilled from Na/benzophenone before use, DMF was dried over molecular sieves (3/4 Å) for at least 3 days, and Et_3N was distilled and kept on KOH pellets. 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. For diisopropyl ether (DIP) and dimethoxypropane (DMP), abbreviations are used, while hexanes refer to a petroleum ether isomer mixture with boiling point between 60 and 80 °C.

Lithium picrate was prepared by dissolving LiOH in boiling water and neutralizing the solution with picric acid. After cooling the solution to 5 °C, the excess picric acid was filtered off and the aqueous phase was excessively extracted with CH_2Cl_2 till the organic layer remained colorless. Lithium picrate was obtained after evaporation of the solvent and drying the residue at 100 °C for 48 h.

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, CA) 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 are uncorrected. Mass (FAB) spectra were recorded using *m*-nitrobenzyl alcohol as a matrix. Infrared spectra were recorded at ambient temperature on a FT-IR spectrometer with a DTSG detector and a resolution of 4 cm^{-1} and were corrected for the solvent (CH_2Cl_2). The presence of solvent molecules in analytical samples was confirmed by ^1H NMR spectroscopy. The ^1H NMR, ^{13}C NMR (unless otherwise stated 250 and 62.5 MHz), and ^{31}P NMR spectra (400 MHz) were recorded in $CDCl_3$ at ambient temperature, and the chemical shifts were expressed relative to $CDCl_3$ (at δ 7.26 and 76.91 ppm, respectively, for ^1H and ^{13}C NMR).

Compounds **1**[13] and **10**[5] were prepared according literature procedures.

Tetramethylcavitand 2. A solution of tetramethyloctol **1** (10 g, 12 mmol), CH_2BrCl (13 mL, 0.20 mol), and K_2CO_3 (35.3 g, 0.25 mol) in DMF (600 mL) was stirred at 70 °C overnight. After removal of the solvent in vacuo, the residue was dissolved in CH_2Cl_2 (250 mL) and 2 N HCl (150 mL). The organic layer was separated, washed with 2 N HCl (3 × 100 mL), H_2O (100 mL), and dried over $MgSO_4$. The organic layer was passed through a short silica column (2 cm) eluted with CH_2Cl_2 and then the solvent was removed in vacuo to afford **2** as a slightly yellow powder: yield 9.64 g (92%); mp 135−137 °C (CH_2Cl_2); MS *m*/*z* 872.5 [100%, M^+, calcd 872.5]; ^1H NMR δ 6.97 (s, 4 H), 5.87 (d, 4 H, J = 6.9 Hz), 4.75 (t, 4 H, J = 8.0 Hz), 4.25 (d, 4 H, J = 6.9 Hz), 2.22−2.16 (m, 8 H), 1.97 (s, 12 H), 1.5−1.3 (m, 24 H), 0.90 (t, 12 H, J = 6.9 Hz); ^{13}C NMR δ 153.2, 138.0, 123.6, 117.6, 96.5, 37.0, 10.3. Anal. Calcd for $C_{56}H_{72}O_8$: C, 77.03; H, 8.31. Found: C, 77.16; H, 8.58.

Tetrakis(bromomethyl)cavitand 3. A solution of tetramethylcavitand **2** (10.0 g, 11.5 mmol), recrystallized NBS (9.2 g, 51.5 mmol), and a catalytic amount of AIBN was refluxed in CCl_4 (400 mL) for 5 h. The reaction mixture was allowed to cool to rt, the precipitate was removed by filtration, and the organic layer was washed with H_2O (2 × 100 mL) and dried over $MgSO_4$. Evaporation of the solvent provided the crude product which was recrystallized from CH_2Cl_2/EtOH to afford **3** as a yellowish powder: yield 12.75 g (93%); mp 278−279 °C (CH_2Cl_2/EtOH); MS *m*/*z* 1188.1 [20, M^+, calcd 1188.2], fragmentation peaks indicate loss of bromine during measurement; ^1H NMR δ 7.13 (s, 4 H), 6.02 (d, 4 H, J = 6.7 Hz), 4.77 (t, 4 H, J = 8.0 Hz), 4.55 (d, 4 H, J = 6.8 Hz), 4.41 (s, 8 H), 2.19 (q, 8 H, J = 6.1 Hz), 1.5−1.25 (m, 24 H), 0.90 (t, 12 H, J = 6.8 Hz); ^{13}C NMR δ 153.6, 138.1, 124.5, 121.0, 99.1, 36.9, 26.9, 23.0. Anal. Calcd for $C_{56}H_{68}Br_4O_8 \cdot 0.5CH_2Cl_2$: C, 55.12; H, 5.65. Found: C, 54.83; H, 5.36.

Tetrakis(phthalimidomethyl)cavitand 4. A solution of (bromomethyl)cavitand **3** (1.40 g, 1.18 mmol), phthalimide potassium derivative (1.31 g, 7.07 mmol), and $(C_4H_9)_3P(Br)$-$C_{16}H_{33}$ (0.24 g, 0.47 mmol) in toluene (75 mL) was refluxed for 4 h. The solvent was removed in vacuo and the residue dissolved in CH_2Cl_2 (50 mL), washed with 1 N NaOH (3 × 25 mL), and dried over $MgSO_4$. The solvent was removed in vacuo and the crude product was purified by flash column chromatography (SiO_2, EtOAc/hexanes 50/50) to afford **4** as a white foam: yield 1.24 g (72%); mp 312−314 °C (hexanes/EtOAc), phase transformation at 160−162 °C; MS *m*/*z* 1452.3 [90, M^+, calcd 1452.6]; ^1H NMR δ 7.85−7.80 and 7.72−7.69 (2m, 8 + 8 H), 7.06 (s, 4 H), 5.77 (d, 4 H, J = 7.2 Hz), 4.65 (t, 4 H, J = 7.9 Hz), 4.65 (s, 8 H), 4.42 (d, 4 H, J = 7.3 Hz), 2.25−2.05 (m, 8 H), 1.45−1.15 (m, 24 H), 0.89 (t, 12 H, J = 6.6 Hz); ^{13}C NMR δ 167.9, 153.9, 137.9, 133.9, 132.0 123.3, 121.2, 120.1, 99.6, 36.8. Anal. Calcd for $C_{88}H_{84}N_4O_{16} \cdot 2.5H_2O$: C, 70.53; N, 3.74; H, 5.99. Found: C, 70.56; N, 3.51; H, 6.16.

Tetrakis(aminomethyl)cavitand 5. A solution of (phthalimidomethyl)cavitand **4** (5.02 g, 3.45 mmol) and hydrazine hydrate (3.47 mL, 71 mmol) in a 9/1 mixture of EtOH (450 mL) and THF (50 mL) was refluxed for 4 h. After addition of concentrated HCl (11.9 mL, 143 mmol) the reaction mixture was refluxed for another hour. The solvents were removed in vacuo, 2 N NaOH (100 mL) was added, and the precipitate was filtered off. The residue was washed with H_2O (25 mL) three times, suspended, and evaporated from CH_2Cl_2 (50 mL) to afford **5** as an off-white powder: yield 3.03 g (94%); mp 175−177 °C (dec) (CH_2Cl_2); MS *m*/*z* main peak 871.1 [100, $(M - CH_2NH_2 - 2NH_2)^+$, calcd 870.5], fragmentation peaks show loss of NH_2 and CH_2NH_2 during measurement; ^1H NMR δ 7.03 (s, 4 H), 5.90 (d, 4 H, J = 6.8 Hz), 4.75 (t, 4 H, J = 7.7 Hz), 4.35 (d, 4 H, J = 6.9 Hz), 3.61 (s, 8 H), 2.25−2.15 (m, 8 H), 1.6−1.2 (m, 24 H), 0.91 (t, 12 H, J = 6.5 Hz); ^{13}C NMR δ 153.0, 138.2, 128.9, 119.0, 99.3, 37.0, 36.0. Anal. Calcd for $C_{56}H_{76}N_4O_8 \cdot 1.5H_2O$: C, 70.04; N, 5.83; H, 8.29. Found: C, 69.92; N, 5.60; H, 8.42.

Tetrakis[(propylamino)methyl]cavitand 6. A solution of (bromomethyl)cavitand **3** (1.02 g, 0.86 mmol) in *n*-propylamine (25 mL) was stirred for 15 min at rt. Subsequently the *n*-propylamine was evaporated and the residue dissolved in CH_2Cl_2 (50 mL), whereupon the organic layer was washed with 0.5% aqueous $NaHCO_3$ (3 × 25 mL) and dried over Na_2SO_4. Evaporation of the solvent afforded **6** as a yellowish foam: yield 0.92 g (97%); mp 68−70 °C (DIP); MS *m*/*z* 1102.1 [10, $(M + H)^+$, calcd 1102.6], spectrum shows fragmentation with loss of Pr, NHPr, and CH_2NHPr during measurement; ^1H NMR $\boldsymbol{\delta}$ 7.04 (s, 4 H), 5.86 (d, 4 H, J = 6.9 Hz), 4.73 (t, 4 H, J = 8.0 Hz), 4.32 (d, 4 H, J = 6.9 Hz), 3.53 (s, 8 H), 2.53 (t, 8 H, J = 7.2 Hz), 2.20 (q, 8 H, J = 6.1 Hz), 1.5−1.1 (m, 8 H + 24 H), 0.95−0.9 (m, 12 H + 12 H); ^{13}C NMR $\boldsymbol{\delta}$ 153.5, 138.0, 126.4, 119.2, 99.4, 51.8, 43.3, 37.0, 11.8. Anal. Calcd for $C_{68}H_{100}N_4O_8 \cdot H_2O$: C, 72.95; H, 9.18; N, 5.00. Found: C, 72.85; H, 9.35; N, 4.76.

Tetrakis(chloroacetamido)cavitand 7a. To a solution of (aminomethyl)cavitand **5** (1.00 g, 1.07 mmol) and Et_3N (2.38 mL, 17.14 mmol) in CH_2Cl_2 (100 mL) was added chloroacetyl

chloride (1.02 mL, 12.86 mmol), whereupon the reaction mixture was refluxed for 3 h. Subsequently, the solution was washed with 1 N HCl (2 × 5 mL), H_2O (2 × 25 mL), 2 N NaOH (3 × 25 mL), and 1 N HCl (2 × 25 mL) and dried over $MgSO_4$. Evaporation of the solvent afforded **7a** as an off-white powder: yield 1.24 g (93%); mp 281−283 °C (DMP); MS *m*/*z* 1259.6 [30, $(M + Na)^+$, calcd 1259.8]; ^{1}H NMR δ 7.09 (s, 4 H), 6.95 (t, 4 H, J = 5.2 Hz), 5.98 (d, 4 H, J = 7.3 Hz), 4.75 (t, 4 H, J = 7.9 Hz), 4.38 (d, 4 H, J = 7.3 Hz), 4.33 (d, 8 H, J = 4.5 Hz), 4.00 (s, 8 H), 2.20 (q, 8 H, J = 5.9 Hz), 1.4−1.25 (m, 24 H), 0.92 (t, 12 H, J = 6.8 Hz); ^{13}C NMR δ 165.6, 153.6, 138.2, 123.0, 120.1, 99.9, 42.6, 36.9. Anal. Calcd for $C_{64}H_{80}Cl_4N_4O_{12}$·1.5$H_2O$: C, 60.71; H, 6.61; N, 4.42. Found: C, 60.73; H, 6.47; N, 4.19.

Tetrakis[(*N*-propylchloroacetamido)methyl]-cavitand 7b. To a solution of [(propylamino)methyl]cavitand **6** (1.00 g, 0.908 mmol) and Et_3N (2.01 mL, 14.52 mmol) in CH_2Cl_2 (100 mL) was added chloroacetyl chloride (0.8 mL, 10.89 mmol), whereupon the reaction mixture was refluxed for 4 h. The solution was washed with 1 N HCl (3 × 25 mL) and 2 N NaOH (3 × 25 mL), a small amount (3 mL) of DMP was added, and the solvent was removed in vacuo. The crude product was purified by flash column chromatography (SiO_2, CH_2Cl_2/MeOH gradient 100/0 to 96/4) to afford **7b** as a white powder: yield 1.15 g (90%); mp 238−240 °C (CH_2Cl_2/MeOH); MS *m*/*z* 1429.5 [85, $(M + Na)^+$, calcd 1429.5]; ^{1}H NMR (major conformation,[39] 400 MHz) δ 7.13 (d, 4 H, J = 2.0 Hz), 5.80 (d, 4 H, J = 6.4 Hz), 4.72 (t, 4 H, J = 7.9 Hz), 4.48 and 4.40 (2d, 4 H, J = 6.5 Hz), 4.42 (dd, 8 H, 2 × J = 4.3 Hz), 4.05 (s, 8 H), 3.21−3.12 (m, 8 H), 2.25−2.20 (m, 8 H), 1.45−1.40 (m, 8 H), 1.50−1.30 (m, 24 H), 0.95−0.80 (m, 24 H); ^{13}C NMR δ 166.2, 154.2, 137.9, 122.5, 119.8, 99.5, 48.9, 41.6, 36.8. Anal. Calcd for $C_{76}H_{104}Cl_4N_4O_{12}$: C, 64.86; H, 7.45; N, 3.98. Found: C, 64.74; H, 7.47; N, 3.83.

General Procedures. Arbusov Reactions. In an open flask the starting material was dissolved/suspended in a small amount of the Arbusov reagent while the temperature was gradually increased from 100 to 150 °C, whereupon the mixture was stirred for 15−60 min. After cooling of the reaction mixture to rt, DIP was added till a precipitate was formed. The precipitate was filtered, thoroughly washed with DIP, and purified by column chromatography (Sephadex LH-20, MeOH/CH_2Cl_2 1/1).

Amidation with *p*-Nitrophenyl (Diphenylphosphoryl)-acetate (10). A solution of the [(alkylamino)methyl]cavitand and *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**) in toluene was refluxed for 6−23 h. After the reaction mixture was cooled to rt, the solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2 (25 mL), washed with 5% aqueous $NaHCO_3$ (3 × 10 mL), 1 N HCl (10 mL), and 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).

Tetrakis[diphenyl[(*N*-methylcarbamoyl)methyl]phosphine oxide]cavitand 8a. **Method A.** The general procedure for the Arbusov reaction was applied to [(chloroacetamido)-methyl]cavitand **7a** (60 mg, 48.4 μmol) and ethyl diphenylphosphinite (0.2 mL) to afford **8a** as a yellowish powder (yield 72 mg, 78%). **Method B.** The general procedure for the amidation was applied to (aminomethyl)cavitand **5** (0.10 g, 0.11 mmol) and *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**) (0.18 g, 0.48 mmol). After refluxing for 4 h in toluene (10 mL) **8a** was obtained as a slightly yellow powder: yield 0.20 g (98%); mp 138−140 °C (DIP); MS *m*/*z* 1924.8 [100, $(M + Na)^+$, calcd 1925.0]; IR ν 1671 cm^{-1} (C═O stretch); ^{1}H NMR (400 MHz) δ 7.72−7.64 and 7.48−7.36 (2m, 16 + 24 H), 7.21 (bs, 4 H), 7.06 (s, 4 H), 5.55 (d, 4 H, J = 7.2 Hz), 4.72 (t, 4 H, J = 7.9 Hz), 4.43 (d, 4 H, J = 7.9 Hz), 4.22 (d, 8 H, J = 4.5 Hz), 3.24 (d, 8 H, $^2J_{PH}$ = 13.7 Hz), 2.25−2.05 (m, 8 H), 1.45−1.15 (m, 24 H), 0.91 (t, 12 H, J = 6.9 Hz); ^{13}C NMR δ 164.2, 164.1, 153.9, 138.0, 132.5−128.7, 123.7, 119.9, 100.1, 39.3, 36.8, 34.0; ^{31}P NMR δ 29.66. Anal. Calcd for $C_{112}H_{120}N_4O_{16}P_4$·4$H_2O$: C, 68.14; H, 6.54; N, 2.84. Found: C, 67.98; H, 6.52; N, 2.60.

Tetrakis[diphenyl[(*N*-methyl-*N*-propylcarbamoyl)-methyl]phosphine oxide]cavitand 8b. Method A. The general procedure for the Arbusov reaction was applied to [(*N*-propylchloroacetamido)methyl]cavitand **7b** (117 mg, 83.1 μmol) and ethyl diphenylphosphinite (0.7 mL) to afford **8b** as a slightly yellow foam (yield 137 mg, 80%). **Method B.** The general procedure for the amidation was applied to [(propylamino)methyl]cavitand **6** (152 mg, 138 μmol) and *p*-nitrophenyl (diphenylphosphoryl)acetate (**10**) (0.43 g, 0.82 mmol). After refluxing for 23 h in toluene (20 mL) the residue was purified by chromatography without previous washings to afford **8b** as a yellowish oil which was redissolved and evaporated from CH_2Cl_2/CH_3CN till a light-yellow powder was obtained: yield 0.27 g (94%); mp 126−128 °C (CH_2Cl_2/CH_3-CN); MS *m*/*z* 2093.5 [85, $(M + Na)^+$, calcd 2093.3]; IR ν 1635 cm^{-1} (C═O stretch); ^{1}H NMR (major conformation,[39] 400 MHz) δ 7.84−7.71 and 7.43−7.28 (2m, 16 + 24 H), 6.98 (d, 4 H, J = 1.9 Hz), 5.55 (d, 4 H, J = 7.6 Hz), 4.57 (t, 4 H, J = 7.9 Hz), 4.50−4.40 (m, 4 H), 4.35−4.15 (m, 4 H), 4.16 (d, 4 H, J = 7.6 Hz), 4.10−4.00 (m, 4 H), 3.95−3.80 (m, 4 H), 3.75−3.60 (m, 8 H), 3.10−3.00 (m, 8 H), 2.15−2.00 (m, 8 H), 1.45−1.20 (m, 24 H), 1.0−0.80 (m, 12 H), 0.80−0.70 (m, 12 H); ^{13}C NMR (100 MHz) δ 165.0, 154.1, 137.8, 132.0, 131.9, 131.3, 131.2, 128.5, 128.4, 128.3, 122.6, 99.0, 46.5, 38.7, 38.1, 36.7, 31.9, 30.0; ^{31}P NMR δ 28.67. Anal. Calcd for $C_{124}H_{144}N_4O_{16}P_4$·2$H_2O$: C, 70.71; H, 7.08; N, 2.66. Found: C, 70.53; H, 7.06; N, 2.70.

Tetrakis[diethyl [(*N*-methylcarbamoyl)methyl]phosphonate]cavitand 9a. The general procedure for the Arbusov reaction was applied to [(chloroacetamido)methyl]cavitand **7a** (125 mg, 101 μmol) and triethyl phosphite (1.5 mL) to afford **9a** as a yellowish powder after precipitation: yield 94 mg (57%); mp 121−123 °C (DIP); MS *m*/*z* 1668.1 [100, $(M + Na)^+$, calcd 1668.6]; ^{1}H NMR (400 MHz) δ 7.89 (bs, 4 H), 7.14 (s, 4 H), 5.95 (d, 4 H, J = 7.9 Hz), 4.76 (t, 4 H, J = 8.0 Hz), 4.47 (bs, 8 H), 4.18 (d, 4 H, J = 7.8 Hz), 4.02 (bs, 16 H), 2.90 (d, 8 H, $^2J_{PH}$ = 21.1 Hz), 2.19 (q, 8 H, J = 6.2 Hz), 1.45−1.2 (m, 24 H), 1.25−1.1 (m, 24 H), 0.89 (t, 12 H, J = 6.8 Hz); ^{13}C NMR δ 163.4, 154.2, 138.1, 124.8, 119.8, 101.6, 62.6, 36.8, 35.8, 33.6, 31.9, 15.6; ^{31}P NMR δ 23.09. Anal. Calcd for $C_{80}H_{120}N_4O_{24}P_4$·$H_2O$: C, 57.75; H, 7.39; N, 3.37. Found: C, 57.60; H, 7.39; N, 3.25.

Tetrakis[diethyl [(*N*-methyl-*N*-propylcarbamoyl)methyl]phosphonate]cavitand 9b. The general procedure for the Arbusov reaction was applied to [(*N*-propylchloroacetamido)methyl]cavitand **7b** (175 mg, 124 μmol) and triethyl phosphite (1.5 mL). After cooling of the mixture to rt, most of the triethyl phosphite was removed in vacuo and the residue was purified twice by column chromatography. Removal of the solvent gave **9b** as a slightly yellowish foam: yield 0.21 g (93%); mp 74−76 °C (CH_2Cl_2/MeOH); MS *m*/*z* 1836.3 [100, $(M + Na)^+$, calcd 1837.0]; ^{1}H NMR (major conformation,[39] 400 MHz) δ 7.06 (d, 4 H), 5.86 (d, 4 H, J = 7.2 Hz), 4.69 (t, 4 H, J = 7.2 Hz), 4.25−4.15 (m, 12 H), 4.15−4.00 (m, 16 H), 3.25−3.10 (m, 8 H), 3.02 (d, 8 H, $^2J_{PH}$ = 22.0 Hz), 2.25−2.10 (m, 8 H), 1.45−1.10 (m, 56 H), 0.90−0.70 (m, 24 H); ^{13}C NMR (100 MHz) δ 164.2, 154.0, 137.7, 122.6, 119.6, 99.2, 62.3, 49.0, 38.9, 36.5, 33.6, 31.7, 16.0; ^{31}P NMR δ 21.81. Anal. Calcd for $C_{92}H_{144}N_4O_{24}P_4$·$CH_2Cl_2$: C, 58.82; H, 7.64; N, 2.95. Found: C, 59.00; H, 7.86; N, 3.11.

Tetrakis(diphenylmethylphosphine oxide)cavitand 11a. The general procedure for the Arbusov reaction was applied to (bromomethyl)cavitand **3** (106 mg, 89.2 μmol) and ethyl diphenylphosphinite (0.8 mL) to afford **11a** as a white powder: yield 117 mg (78%); mp 158−160 °C (CH_2Cl_2/MeOH); MS *m*/*z* 1673.9 [100, M^+, calcd 1673.7]; ^{1}H NMR δ 7.7−7.65 and 7.50−7.36 (2m, 16:24 H), 6.81 (s, 4 H), 5.23 (d, 4 H, J = 6.9 Hz), 4.39 (t, 4 H, J = 7.8 Hz), 4.20 (d, 4 H, J = 7.1 Hz), 3.46 (d, 8 H, $^2J_{PH}$ = 14.7 Hz), 2.1−1.95 (m, 8 H), 1.4−1.15 (m, 24 H), 0.88 (t, 12 H, J = 6.9 Hz); ^{13}C NMR δ 153.3, 153.2, 137.4, 133.9, 132.5−128.7, 118.8, 98.8, 36.8. Anal. Calcd for $C_{104}H_{108}O_{12}P_4$·CH_2Cl_2: C, 71.70; H, 6.30. Found: C, 71.76; H, 6.35.

Tetrakis(diethyl methylphosphonate)cavitand 11b. The general procedure for the Arbusov reaction was applied to (bromomethyl)cavitand **3** (167 mg, 140 μmol) and triethyl phosphite (0.5 mL) to afford **11b** as a colorless oil: yield 188 mg (94%); MS *m*/*z* 1439.5 [100, $(M + Na)^+$, calcd for $C_{72}H_{108}O_{20}P_4$·Na: 1440.5]; ^{1}H NMR δ 6.99 (s, 4 H), 5.81 (d, 4 H, J = 7.3 Hz), 4.69 (t, 4 H, J = 7.6 Hz), 4.36 (d, 4 H, J = 7.3 Hz), 4.02 (dq, 16 H, J = 7.2 Hz, J = 7.2 Hz), 2.94 (d, 8 H, $^2J_{PH}$

(39) Only the data for the major conformer are presented.

= 22.5 Hz), 2.2−2.05 (m, 8 H), 1.3−1.1 (m, 24 H), 1.18 (t, 24 H, J = 7.0 Hz), 0.84 (t, 12 H, J = 6.9 Hz); ^{13}C NMR δ 153.6, 153.4, 137.8, 137.6, 119.0, 118.7, 118.6, 99.6, 62.1, 62.0, 36.8.

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 3.0 and adjusted to it 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 experiments were carried out at pH 3.0, imposed by the need to ensure that the added picrate is predominantly present in its anionic form (the dissociation constant of picric acid[40] is pK_a = 0.38) and that the metal cations employed do not undergo hydrolysis.[41] 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 (10−200 μL) of a radiotracer solution to the respective salt solutions. The spicked Fe^{3+} 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 0.9×10^{-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 into a glass stoppered glass tube and magnetically stirred at ambient temperatures (22−24 °C) for at least 1 h to ensure complete settling of the equilibrium.[42] Preliminary experiments had shown that an equilibrium generally sets within less than 10 min. The solutions were disengaged by centrifugation (1600 rpm for 5 min; 10 min in the case of the Fe^{3+} extraction experiments) and equal aliquots (0.5 mL) of the organic and aqueous phases were pipetted out. The γ-activity in both samples was determined with well type NaI(Tl) scintillation counters, except for the uranium experiments, where liquid scintillation counting was used. The percentage of the cation extracted in the organic phase (%$E = E \times 100\%$), defined as the ratio of the activity in the organic phase (A_o) and the total activity in both the organic and the aqueous phase (A_a), is expressed by eq 2:

$$\%E = \left[\frac{A_o}{A_a + A_o}\right] \times 100\% \qquad (2)$$

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 preequilibrated 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,[43] slight extraction (%$E_{Eu} \sim 0.4$) was observed in blank experiments. The reported extraction percentages are the average of at least three (metal extraction) or two (concentration variation) experiments. The error in the reported extraction percentages is <2%E (<5%E for Fe^{3+}). Especially in the >90% extraction region, the error in the resulting distribution coefficient may become quite large, as an error of 1%E can give deviations of 20% in D_M, and thus also even larger errors in the calculated separation factors. The errors in the K_{ex}^1 values are less than 5%.

Determination of Extraction Coefficients (K_{ex}). The extraction of metal cations (M^{n+}) accompanied by n anions and p neutral organic ligands (L) can be described by general expression 3:

$$[M^n]_w + n \times [X^-]_w + p \times [L]_o \rightleftarrows [M{\cdot}X_n{\cdot}L_p]_o \qquad (3)$$

Where M = Eu^{3+}, X = picrate, n = 3, p = 1, 2, ... , and the subscripts o and w denote the presence of the species in the organic or aqueous phase. Assumptions are made that the partition of the ligand to the aqueous phase is negligible ($[L]_w \sim 0$). The presence in the organic phase of $M(Pic)_3$ and $M{\cdot}X'_3{\cdot}L_p$ species (with $X' = NO_3^-$ or Cl^-; the initial anions of the salts) and the extraction of mixed complexes ($M{\cdot}X_n{\cdot}X'_{(3-n)}{\cdot}L_p$) is also negligible, as was confirmed by blank experiments. The extraction coefficient for the p:1 complexation K_{ex}^p is then described by expression 4:

$$K_{ex} = \frac{[Eu{\cdot}Pic_3{\cdot}L_p]_o}{[Eu^{3+}]_w \times [Pic^-]_w^3 \times [L]_o^p} \qquad (4)$$

The distribution coefficient D is defined by general expression 5 as the ratio of the metal concentration in the organic and in the aqueous phase. In the case of europium extraction and under the conditions that only one complex (p:1 stoichiometry, ligand-to-metal ratio) is present and Eu^{3+} is unassociated in the aqueous phase (thus neglecting $EuPic^{2+}$ and $Eu(Pic)_2^+$ species), the relation for D_{Eu} follows from the general expression:

$$D_M = \frac{\sum(M)_o}{\sum(M)_w} \left(= \frac{[Eu{\cdot}Pic_3{\cdot}L_p]_o}{[Eu^{3+}]_w}\right)_{Eu;\ p:1\ complex} \qquad (5)$$

Substitution of eq 4 in eq 5 and taking logarithms gives an equation in which the dependence of the log D is described as a function of the K_{ex}^p and the concentrations of the anion and the ligand:

$$\log D_{Eu} = \log K_{ex}^p + 3 \times \log [Pic^-]_w + p \times \log[L]_o \qquad (6)$$

Under the assumption that $[Pic^-]_w \approx [Pic^-]_{w,i} = 10^{-2}$ M, a plot of log D vs log $[L]_o$ should be linear with a slope of p; where p indicates the number of ligand molecules involved per cation in the extracted species. The intercept of the plots with the log D-axis equals log K_{ex}^p + 3 log $[Pic^-]_{w,i}$, which allows the determination of the value of the extraction coefficient.

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