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PAPER

Synthesis and evaluation of ligands with mixed amide and phosphonate, phosphinoxide, and phosphonothioate sites for An(III)/Ln(III) extraction

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Various organophosphorus ligands with a combination of different donor sites were synthesized and evaluated by solvent extraction studies for the complexation of Am(III)/Eu(III). Among the ligands with a glycolamide backbone, those with mixed amide and P═O donor sites and a central oxygen or nitrogen atom showed a reasonable extraction of Am(III) and Eu(III). Ligands with a central oxygen atom exhibited selectivity towards Eu(III), and those with a central nitrogen atom towards Am(III). Ligands with P═S donor sites and a glycolamide backbone did not show any reasonable extraction. Amongst the ligands with a malonamide backbone, high extraction efficiency was observed for the ligand with electron-rich substituents on phosphorus, however, with almost no discrimination between Am(III) and Eu(III). The extraction efficiency of different ligands towards Eu(III) was confirmed by microcalorimetry.

Introduction

Spent fuel arising from the civil use of nuclear power generation is composed mainly of residual uranium (~95 wt%) and a small amount of the highly radiotoxic transuranium elements, plutonium (~1 wt%) and the minor actinides (neptunium, americium and curium, 0.1%). The fission products (~4 wt%) contribute mainly to the short-term (up to 300 years) radiotoxicity and heat production of the waste. Solvent extraction, in the form of the well-known PUREX process (plutonium–uranium reduction–extraction), has been practiced at the industrial scale in the nuclear industry for over 6 decades for the recovery of uranium and plutonium. The amount of radioactive nuclear waste and its long-term radiotoxicity can be further reduced by the partitioning (P) and transmutation (T) strategy.[1] In this strategy the long-lived radionuclides, mainly the minor actinides (MAs) are recovered and converted into short-lived or stable isotopes by irradiation in a dedicated reactor. MA recycling by P and T could significantly change the challenges for the storage of nuclear waste by reducing the heat load, the radiotoxicity and the overall "half-life" of the waste to be buried. The separation of the minor actinides from the lanthanides is a crucial step in this strategy, since the lanthanides exhibit a large neutron capture cross-section and hinder an efficient transmutation of the actinides. The chemical similarity of the trivalent actinides and lanthanides makes this separation very difficult.

Various processes for the co-extraction of actinides (An) and lanthanides (Ln) were developed in recent years, like the TRUEX[2] (based on CMPO (carbamoylmethylphosphinoxide)), TRPO[3] (based on trialkyl phosphinoxide), DIDPA[4] (based on diisodecyl phosphoric acid), and DIAMEX[5] (based on diamide extraction) processes. Different types of ligands for the separation of actinides and lanthanides have been developed as described in recent reviews.[6–9]

During the 1980s, the family of malonamides was developed for the extraction of An(III)/Ln(III) from high level liquid fission product solutions.[10] Structural optimizations ultimately led to the DIAMEX reference compound *N,N′*-dimethyl-*N,N′*-dioctylhexylethoxy malonamide (DMDOHEMA).[5,11]

In the early 1990s, Stephan *et al.*[12] reported on the extraction of different metal ions using multidentate ligands such as diglycolamides (DGA).[13] The DGA substance class with an ether group between both amide functions resembles the malonamides. During the late 1990s, Sasaki and Choppin recognized that these ligands are suitable for extracting actinides from acidic waste solutions.[14,15]

Multifunctional neutral organophosphorus compounds are already known as attractive extracting agents for a long time.[16] A number of ligands containing phosphoryl groups exhibit remarkable extraction and complexation properties towards actinides and lanthanides,[17] *e.g.* the CMPOs. It should be noted that malonamide[10] and CMPO[2] have a similar backbone structure, except that malonamide contains two amide groups and CMPO contains one amide and one phosphinoxide as donating groups. It was pointed out by Musikas that extractant molecules containing nitrogen or sulfur functionalities, which are softer than oxygen donors, offer a great potential to achieve

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the wanted discrimination between An(III) and Ln(III).[18] A number of P═S containing ligands are known to be selective for An(III) compared to Ln(III) *e.g.* Cyanex 301[19] and aromatic dithiophosphinic acids.[20,21]

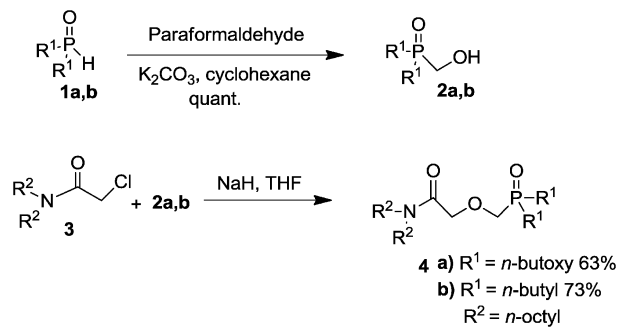
Based on the above mentioned complexing properties of ligating sites in known extractants, the main objective of the present work is to develop novel ligands, a sort of hybrids, in which these sites are combined in a different way on known ligand backbones. The synthesis and extraction properties will be described for both di- and tripodal ligands containing amide and/or phosphinoxide or (thio)phosphonate moieties. This paper focuses on the synthesis and characterization of these ligands. The complexation thermodynamics and complex stoichiometry of Eu(III) with several novel ligands are investigated using microcalorimetry. The performance of the novel ligands is furthermore tested in solvent extraction studies using trace amounts of Am(III) and Eu(III).

Results and discussion

Synthesis

Mixed amides and phosphonates, phosphinoxides with central oxygen. The CMPO type of ligands contain one amide and one phosphinoxide donor group and show a high affinity for hexa-, tetra-, and trivalent actinides including the lanthanides over most non-Ln fission products. The well-known TODGA (*N,N,N′,N′*-tetra-*n*-octyl diglycolamide) exhibits a better extraction efficiency,[13,22] however, showing pronounced selectivity for Eu(III) over Am(III) from HNO_3 medium. Therefore, the TODGA structure was modified by replacing one of its amide group with P═O donors to give **4a,b**. A further modification involves the replacement of the central oxygen with a nitrogen atom, because of its softer donor character, to afford **7a,b**.

The synthesis of the mixed ligands phosphonate-*O*-acetamide (**4a**) and phosphinoxide-*O*-acetamide (**4b**) is summarized in Scheme 1. Reaction of di-*n*-butylphosphinoxide (**1b**) with paraformaldehyde using K_2CO_3 as a base in cyclohexane gave the (hydroxymethyl)phosphinoxide **2b** in quantitative yield, analogous to a procedure for **2a**.[23] Both **2a** and **2b** were reacted with 2-chloro-*N,N*-dioctylacetamide (**3**) in the presence of NaH to get the desired ligands **4a** and **4b** in 63% and 73% yield, respectively. The formation of **4a,b** clearly followed from their ^{1}H NMR spectra by the shift of the peak at 4.05 ppm for the $C(O)CH_2Cl$ group in **3** to 4.29 ppm (**4a**) and 4.17 ppm (**4b**) for the $C(O)CH_2O$ hydrogens.



Scheme 1

The mass spectra show peaks at m/z 506.4 $[M + H]^+$ and m/z 474.4 $[M + H]^+$ for **4a** and **4b**, respectively.

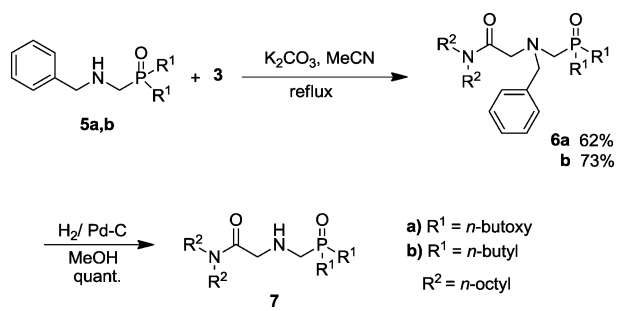
Mixed amides and phosphonates, phosphinoxides with central nitrogen. The known compounds **5a,b** were reacted with 2-chloro-*N,N*-dioctylacetamide (**3**) to afford benzylacetamidephosphonate **6a** and benzylacetamidephosphinoxide **6b** in 62% and 73% yield, respectively. In the ^{1}H NMR spectra the peak for the $C(O)CH_2Cl$ group in **3** has shifted from 4.05 ppm to 3.81 ppm and 3.94 ppm in **6a** and **6b**, respectively. The peak for the benzylic hydrogens is present at 3.53 ppm in **6a** and at 3.60 ppm in **6b**.

In the next step the benzyl group in **6a,b** was cleaved by 5% Pd/C in ethanol under a hydrogen atmosphere to afford phosphonate-*N*-acetamide **7a** and phosphinoxide-*N*-acetamide **7b** in quantitative yields (Scheme 2). The cleavage of the benzyl group in **6a,b** clearly followed from the disappearance of the peaks in the aromatic region in the ^{1}H NMR spectra. In addition, the doublet for the PCH_2N hydrogens shifted from 3.21 ppm in **6a** to 3.03 ppm in **7a** and from 3.06 ppm in **6b** to 3.00 ppm in **7b**.

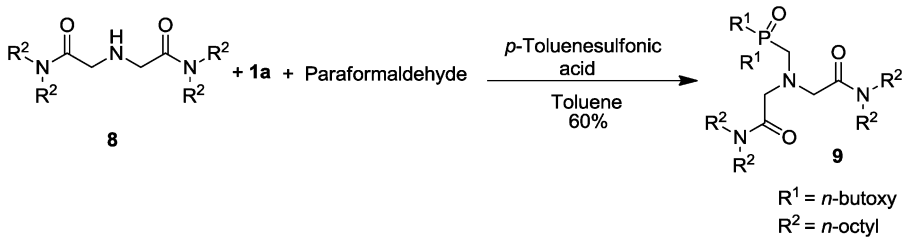
Tripodal mixed amides and phosphonates. Previously, we reported that a tripodal ligand with all amide donor groups showed interesting extraction properties with selectivity for Am(III) over Eu(III).[24] In this study one and two amide groups were replaced by phosphonate groups to give tripodal ligands **9** and **13**, respectively.

Tripodal diacetamidephosphonate **9**, containing one phosphonate and two amide groups, was synthesized by reaction of azanediylbis(*N,N*-dialkylacetamide) (**8**) with di-*n*-butylphosphite (**1a**) in the presence of paraformaldehyde and *p*-toluenesulfonic acid in toluene in 60% yield by an analogous procedure as described for aminomethylphosphinoxides[25] (Scheme 3). The ^{1}H NMR spectrum shows the characteristic PCH_2N doublet at 3.31 ppm. In the mass spectrum the parent peak is found at m/z 786.7 $[M + H]^+$.

For the synthesis of tripodal ligand **13**, containing one amide and two phosphonate groups, benzylamine (**10**), paraformaldehyde, and di-*n*-butylphosphite (**1a**) were reacted in toluene by the same procedure[25] to afford benzyldiphosphonate **11** in 72% yield. The benzyl group in **11** was hydrogenolyzed in ethanol using 10% Pd/C to give aminodiphosphate **12** in quantitative yield. The formation of **12** followed by the disappearance of the protons in the aromatic region in the ^{1}H NMR spectrum; the doublet for the PCH_2N group was shifted from 3.16 ppm in **11** to 3.11 ppm in **12**. Finally, aminodiphosphate **12** was reacted with 2-chloro-*N,N*-dioctylacetamide (**3**) in acetonitrile to give tripodal acetamidediphosphate **13** in 78% yield (Scheme 4). In the ^{1}H NMR spectrum



Scheme 2



Scheme 3

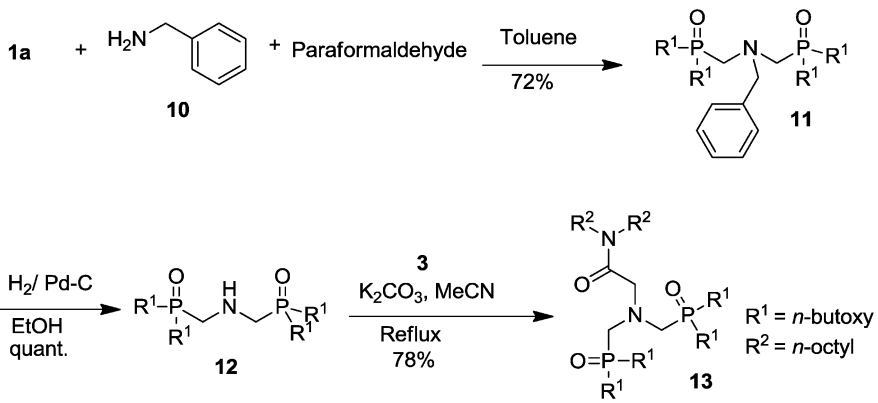
the PCH_2N peak shifted from 3.11 ppm in **12** to 3.35 ppm in **13**, and the $C(O)CH_2Cl$ peak of acetamide **3** shifted from 4.05 ppm to 3.84 ppm for the $C(O)CH_2N$ group. In the mass spectrum the parent peak is found at m/z 711.5 $[M + H]^+$.

P═S containing ligands with a central oxygen atom. As mentioned above, diglycolamides as TODGA have excellent extraction properties with a slight preference for Eu(III) over Am(III). Generally, S donors are selective for Am(III) over Eu(III). Therefore, the amide groups in TODGA were replaced by P═S containing sites to give ligands **16**, **20**, and **23**.

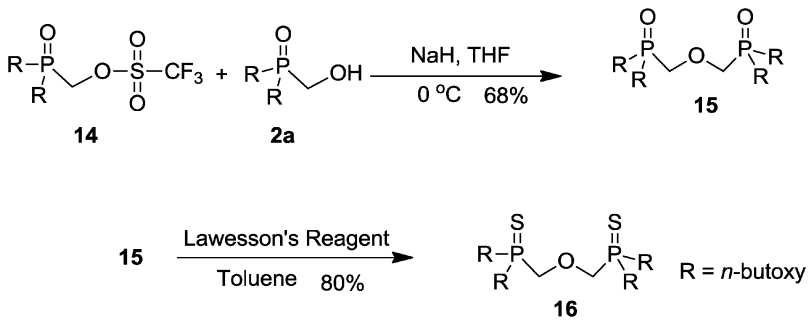
The known (di-*n*-butoxyphosphoryl)methyl trifluoromethanesulfonate **14** was reacted with **2a** using NaH as a base to give the desired diphosphonate **15**. In the ^{1}H NMR spectrum the doublet for the PCH_2O hydrogens at 4.62 ppm in **14** shifted to 3.84 ppm in **15**. The P═O groups in **15** were converted into P═S moieties using Lawesson's reagent to afford **16** in 80% yield (Scheme 5). In this case the PCH_2O protons appeared at 4.07 ppm. Both compounds showed characteristic $[M + H]^+$ peaks in their electrospray mass spectra.

Diphenylphosphine sulfide (**17**) was reacted with paraformaldehyde to get the hydroxymethylated compound **18** in quantitative yield. The introduction of the hydroxymethyl group clearly followed from the peak at 4.42 ppm in its ^{1}H NMR spectrum. Upon conversion of the hydroxyl group in **18** into a tosylate, the resulting tosylate **19** was reacted with **18** in THF using NaH as a base to give the target (oxybis(methylene))bis(diphenylphosphine sulfide) (**20**) in 71% yield (Scheme 6). In the ^{1}H NMR spectrum the peak for the methylene protons in **19** at 4.62 ppm shifted to 4.42 ppm in **20**. The formation of **20** also followed from the correct $[M + H]^+$ peak at m/z 479.1 in the electrospray mass spectrum.

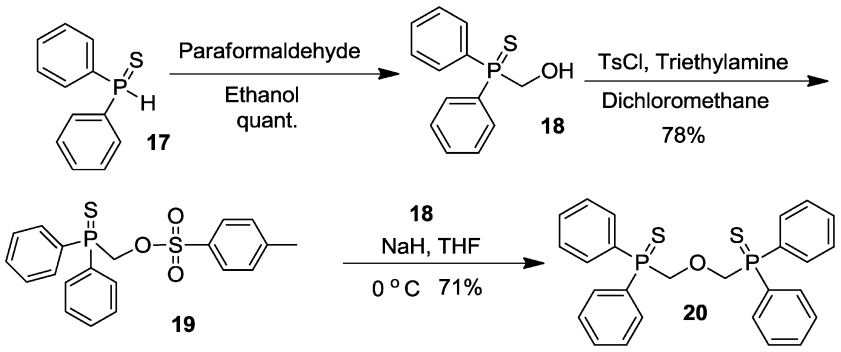
Tosylate **21**, prepared by tosylation of di-*n*-butyl(hydroxymethyl)phosphinoxide (**2b**), was reacted with compound **2b** in the presence of NaH as a base in THF to give (oxybis(methylene))-bis(di-*n*-butylphosphinoxide) (**22**) in 76% yield (Scheme 7). Also in this case a characteristic shift of the PCH_2O methylene resonances occurred in the ^{1}H NMR spectra, *viz.* from 4.15 ppm in **21** to 3.88 ppm in **22**. The P═O groups in **22** were converted into P═S moieties with Lawesson's reagent to



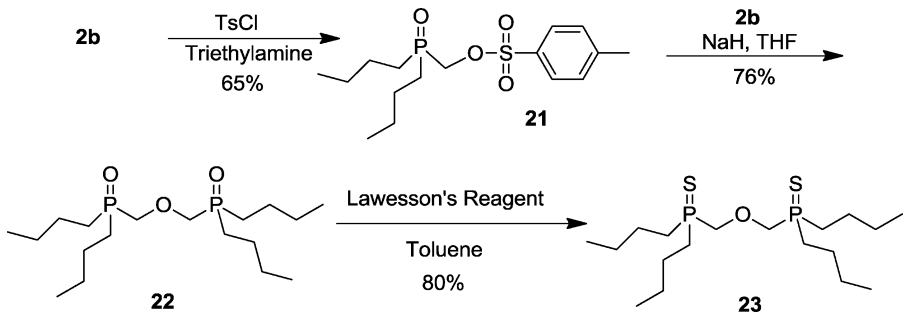
Scheme 4



Scheme 5



Scheme 6



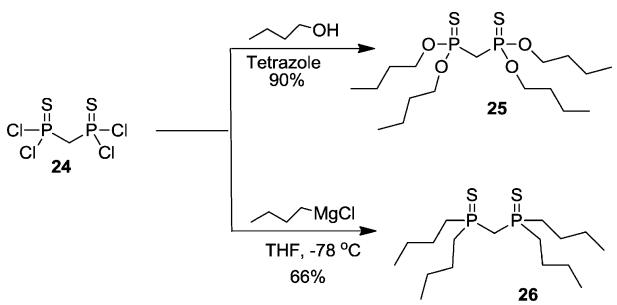
Scheme 7

afford the target ligand **23** in 80% yield. In the ^{1}H NMR spectrum the characteristic methylene protons are present at 3.91 ppm. The formation of these compounds was also confirmed by their $[M + H]^+$ peaks in the electrospray mass spectra.

Methylene-bridged P═S containing ligands

The two lipophilic ligands **25** and **26** can in principle be considered as malonamides of which the amides have been replaced by P═S containing moieties, as described above for TODGA. The synthesis is summarized in Scheme 8.

Methylenediphosphonothioic dichloride (**24**) was reacted with different reagents to get the desired potential ligands **25** and **26**. Stirring of **24** with 1-butanol in the presence of tetrazole gave *O*,*O*,*O*′,*O*′-tetra-*n*-butyl methylenediphosphonothioate (**25**) in 90% yield in an analogous way to that described for the corresponding P═O compounds as a starting material.[26] For the synthesis of methylenebis(di-*n*-butylphosphine sulfide) (**26**) compound **24** was reacted with *n*-butylmagnesium chloride at −78 °C; *n*-butyllithium gave unsatisfactory results. In the ^{1}H NMR spectra the signal for the methylene hydrogens shifted from 4.48 ppm in **24** to 2.99 and 2.46 ppm in **25** and **26**, respectively. These compounds were also characterized by their $[M + H]^+$ peaks in the electrospray mass spectra.



Scheme 8

Extraction results

All the synthesized ligands were tested using liquid–liquid extraction techniques. The extractabilities of Am(III) and Eu(III) by the lipophilic ligands are expressed by the distribution ratios, D_{Am} and D_{Eu} (eqn (1)). The distribution ratios of Am and Eu are plotted as a function of the initial nitric acid concentration.

$$D_M = [M]_{org}/[M]_{aq} \quad (1)$$

The separation factor $SF_{A/B}$ is the ratio of the distribution ratios D_A and D_B (eqn (2)), and describes the selectivity for A over B.

$$SF_{A/B} = D_A/D_B \quad (2)$$

Mixed amides and phosphonates, phosphinoxides with central oxygen or nitrogen. Similar to CMPO, ligands **4a,b** possess two different donating groups: one amide and one phosphonate (**4a**) or phosphinoxide (**4b**) moiety. The extraction of Am and Eu by ligand **4a** increased with increasing nitric acid concentration in the aqueous phase (Fig. 1). Above 1 mol L^{-1} HNO_3, the D values sharply increased reaching values of 4.6 and 0.9 at 4 mol L^{-1} HNO_3 for Eu and Am, respectively.

Phosphinoxide **4b**, which is more similar to CMPO, shows the same extraction behavior as CMPO at lower nitric acid concentrations. However, at $[HNO_3]$ > 0.1 mol L^{-1} the D values are lower. Apparently, the introduction of an oxygen atom between the phosphorus and the alkyl chain in ligand **4a** has a negative influence on the extraction properties compared

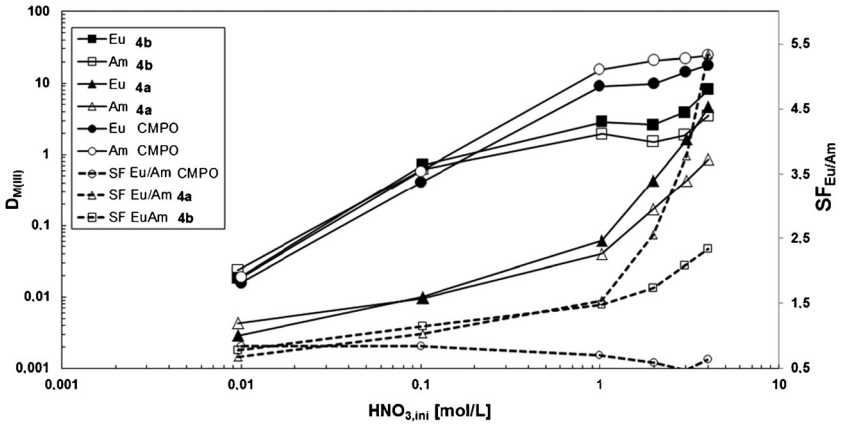


Fig. 1 Nitric acid dependency for the extraction of ^{241}Am and ^{152}Eu by ligands **4a,b** and comparison with CMPO/TBP. Organic phase: 0.1 mol L^{-1} of ligands **4a,b** in TPH (hydrogenated tetrapropene) or 0.2 mol L^{-1} CMPO + 1.4 mol L^{-1} TBP in *n*-dodecane. Aqueous phase: variable concentration of nitric acid, tracers: ^{241}Am and ^{152}Eu, mixing time: 60 min (CMPO: 15 min; enough to reach equilibrium); $T = 22 \pm 1$ °C.

to CMPO. The extraction behavior of these two ligands is similar to that of CMPO, which is a neutral ligand extracting metals by the solvation mechanism.[27] This may suggest the same extraction mechanism in the case of its derivatives **4a,b**. Like other diglycolamide-based ligands[13] **4a,b** exhibit a slight selectivity for Eu over Am. At 4 mol L^{-1} nitric acid concentration the Eu/Am separation factors are 2.5 (ligand **4b**) and 5.5 (ligand **4a**). CMPO shows an opposite selectivity, favoring Am over Eu with Am/Eu separation factors of approximately 2 at 4 mol L^{-1} HNO_3.

The ligands **7a,b** differ from **4a,b** by the presence of a nitrogen instead of an oxygen as the central atom of the back-bone structure. This replacement resulted in a reversed metal extraction behavior (Fig. 2), since the central nitrogen atom is protonated at higher nitric acid concentrations. In the case of both ligands **7a,b**, the metal extractability drastically decreased at nitric acid concentrations >0.1 mol L^{-1}. In addition, a precipitation occurred between the two equilibrated phases at $[HNO_3] \geq 0.1$ mol L^{-1}. The precipitation intensity increased upon increasing the acidity of the aqueous phase. It is assumed that the central nitrogen atom in both ligands is protonated, resulting in precipitation of the HNO_3·ligand. At a nitric acid concentration of 0.01 mol L^{-1}, where the precipitation of the ligands did not take place, the *D* values were higher for ligand **7b** compared to **7a**.

A related lipophilic ligand, also with nitrogen in the center but containing two dioctylacetamide groups, instead of just one, has been studied recently.[24] It did not show any significant extraction of Eu(III) or Am(III) ($D_M < 0.01$). Therefore, we assume that the increase in the *D* values at 0.01 mol L^{-1} HNO_3 in the case of ligands **7a,b** is due to the phosphonate and phosphinoxide groups, respectively.

Tripodal mixed amides and phosphonates. The tripodal ligands **9** and **13** possess an additional third ligating group attached to the central nitrogen, compared to the ligands described above. Ligand **9**, containing two acetamide and one phosphonate group, showed increasing metal extraction at nitric acid concentrations >0.1 mol L^{-1}, although the distribution ratios did not exceed 0.25 at the highest acidity tested (Fig. 3). When one of the acetamide functionalities of **9** was substituted by a phosphonate group (ligand **13**), the metal

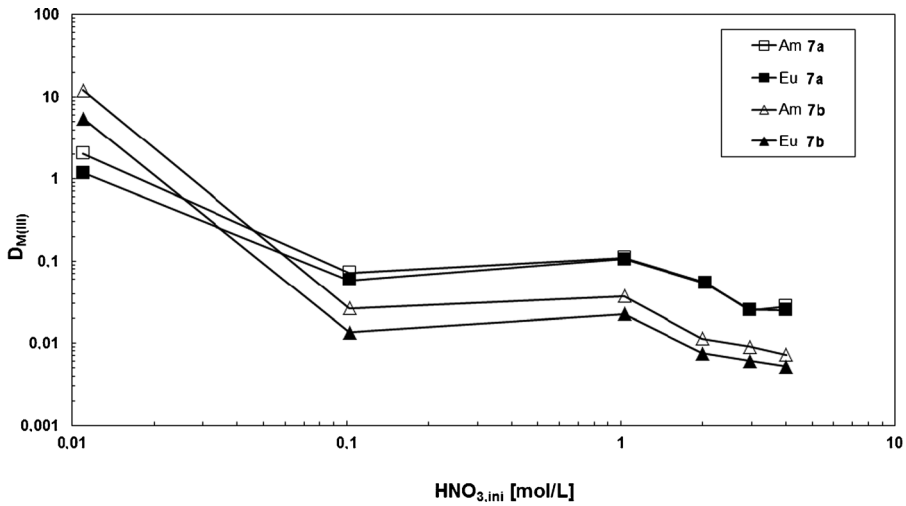


Fig. 2 Nitric acid dependency for the extraction of ^{241}Am and ^{152}Eu by ligands **7a,b**. Organic phase: 0.1 mol L^{-1} ligand in TPH. Aqueous phase: variable concentration of nitric acid, tracers: ^{241}Am and ^{152}Eu, mixing time: 60 min; $T = 22 \pm 1$ °C.

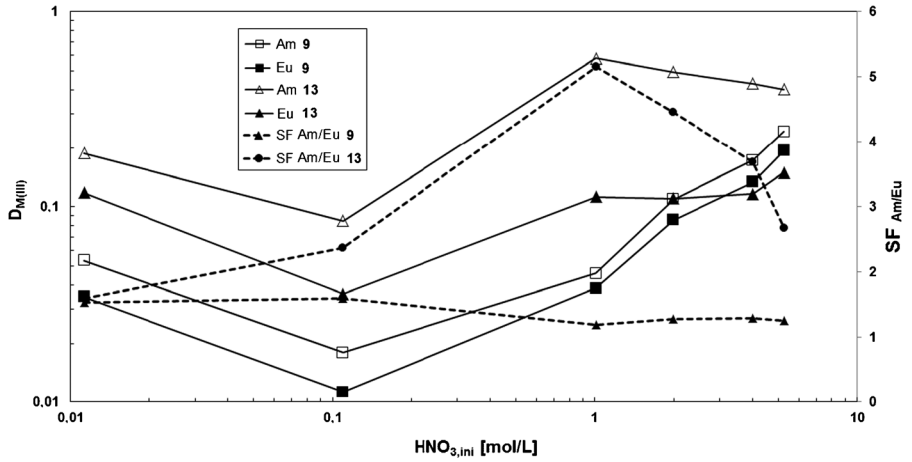


Fig. 3 Nitric acid dependency for the extraction of ^{241}Am and ^{152}Eu by ligands **9** and **13**. Organic phase: 0.1 mol L^{-1} ligand in TPH. Aqueous phase: variable concentration of nitric acid, tracers: ^{241}Am and ^{152}Eu, mixing time: 60 min; $T = 22 \pm 1$ °C.

distribution ratios somewhat increased, especially for Am. The extraction behavior as a function of HNO_3 is more or less reversed compared to that of the related 2,2′,2″-nitrilotris(*N*,*N*-dioctylacetamide) ligand, containing three acetamide groups, which showed higher *D* values at lower acid concentration.[24] It looks like that in the cases of ligands **9** and **13** protonation of the central nitrogen atom is less pronounced than in the mentioned reference ligand.[24] In contrast to the dipodal ligands (**7a,b**), these results clearly show that replacement of an acetamide for a phosphonate group gives rise to a much lower extraction ability at lower nitric acid concentrations. Ligands **9** and **13** show lower extraction at 0.1 compared to 0.01 mol L^{-1} HNO_3 probably due to protonation of the nitrogen atom. The *D* values are increased upon further increase in HNO_3 concentration. It might be due to the fact that nitrogen is not involved in the extraction at higher HNO_3 concentrations, and only three P═O or C═O groups are involved in extraction, where extraction is simply expected to increase upon increase in nitrate ion concentration (metal is extracted in combination with nitrate ions).

P═S containing ligands with a central oxygen atom. As mentioned above, DGA ligands with their three oxygen atoms in the backbone structure are very efficient for trivalent actinide and lanthanide complexation. One may expect selectivity for Am(III) over Eu(III) by replacing C═O by P═S groups in DGA ligands, however, the substitution of the carbonyl oxygens for the softer sulfurs in the lipophilic ligands **16**, **20**, and **23** gave, in addition to low *D* values, no significant separation between Am and Eu. Ligands **20** and **23** even showed no extraction (*D* ratios below the detection limit; see Fig. 4) in the entire tested acidity range. It looks like that there is some influence on the extraction behavior upon the introduction of an oxygen between the butyl chain and the phosphorus into the structure of ligand **23** resulting in ligand **16**, which showed some minor extraction of the metals at low acid concentration (Fig. 4).

Ligand **20** showed a lower metal extractability than **16**, which may result from its poor solubility in TPH. In the extraction experiments the concentration of **20** was 10 times lower than that of **16**.

Methylene-bridged P═S containing ligands

The two lipophilic ligands **25** and **26** represent a good example of the influence of the side chain of the phosphine sulfide on its

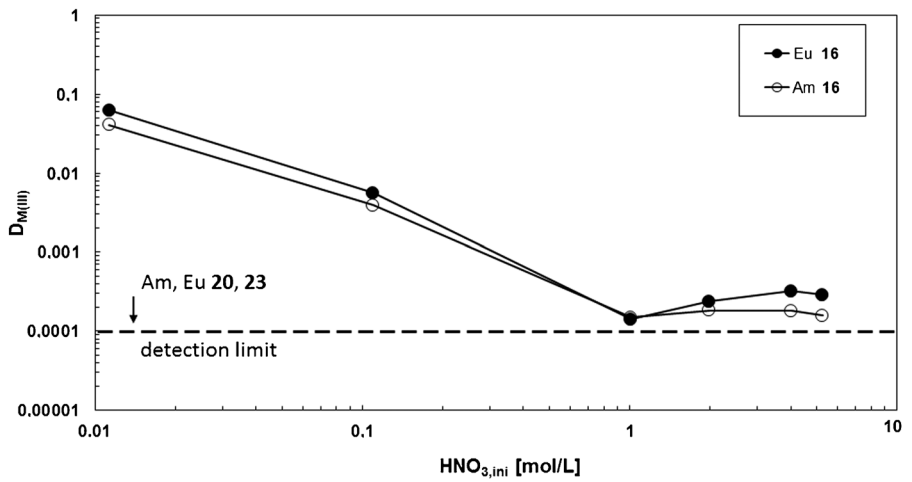


Fig. 4 Nitric acid dependency for the extraction of ^{241}Am and ^{152}Eu by ligand **16**. Organic phase: 0.1 mol L^{-1} **16** in TPH. Aqueous phase: variable concentration of nitric acid, tracers: ^{241}Am and ^{152}Eu, mixing time: 60 min; $T = 22 \pm 1$ °C.

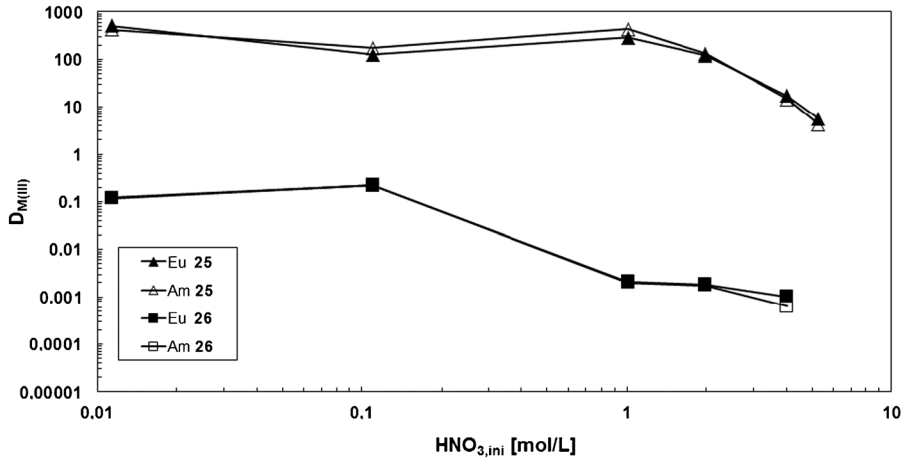


Fig. 5 Nitric acid dependency for the extraction of ^{241}Am and ^{152}Eu by ligands **25** and **26**. Organic phase: 0.1 mol L^{-1} **26** in TPH or 0.09 mol L^{-1} **25** + 0.003 mol L^{-1} 1-octanol in TPH (due to a lower solubility of **25** in pure TPH). Aqueous phase: variable concentration of nitric acid, tracers: ^{241}Am and ^{152}Eu, mixing time: 60 min; $T = 22 \pm 1$ °C.

electronic properties. Ligand **25** has four butoxy groups, thus increasing the basicity of the donor S-atoms, while ligand **26** has four butyl chains, less affecting the basicity. Ligand **26** gave Eu and Am distribution ratios of around 0.1 at low acidity (Fig. 5). Above 0.1 mol L^{-1} HNO_3 the D values even decreased further to 0.001 at 4 mol L^{-1} HNO_3. At an acid concentration of 5 mol L^{-1} precipitation of the ligand occurred, probably due to oxidation of the sulfur.

The butoxy groups of ligand **25** make the sulfur donor atoms much more electron rich as compared to those in **26**, resulting in an increased affinity to the trivalent metals. Distribution ratio values over 100 were obtained in the acidic range 0.01–1 mol L^{-1}, followed by a decrease at higher nitric acid concentration, which may be due to oxidation of the sulfur. Another explanation could be competition between the metal ions and nitric acid extraction. However, after phase contact at 4 and 5 mol L^{-1} HNO_3, a white emulsion between the organic and the aqueous phase was visible in the samples, indicating a low hydrolytic stability. Nevertheless, no losses of Am or Eu were observed.

Cuillerdier *et al.*[10] studied unsubstituted malonamides containing *n*-butyl or *n*-octyl groups to give maximal D_{Am} values of 0.5 and 1.2, respectively, in the acid range of 2–4 mol L^{-1} HNO_3. Compared to the results obtained with ligand **25**, it clearly demonstrates that the replacement of a dialkyl amide for a butyl phosphonothioate moiety leads to higher distribution ratios of Am(III) and Eu(III).

Microcalorimetry

Isothermal microcalorimetry (ITC) experiments were performed to quantitatively study the difference in the binding capacities of ligands **4a**,**b**, **7a**,**b**, **9**, **13**, and **25** towards Eu(III), to determine the stoichiometry of the complexes, and to get insight into the thermodynamics of the ligand : metal complexation. It should be kept in mind, however, that these cannot be directly compared, since the microcalorimetric experiments could not be carried out under similar conditions as the extractions were done due to solubility reasons. ITC experiments were not performed with the other ligands, since they do not exhibit any reasonable extraction. The experiments were performed in acetonitrile, since the ligands were not soluble in water; Eu(III) perchlorate was used because of its solubility in acetonitrile. Therefore a 2 mmol L^{-1} ligand solution was titrated with a 0.066 mmol L^{-1} Eu(III) perchlorate solution, except for ligands **4a,b** where a 1 mmol L^{-1} ligand solution was titrated against 0.033 mmol L^{-1} Eu(III), due to the high binding constants at higher concentrations. The binding constants and the thermodynamic data are summarized in Table 1. Dilution experiments with ligands **4a**,**b**, **7b**, **13**, and **25** showed negligible heat effects, indicating that no aggregation of the ligands takes place under the conditions used. However, in the dilution experiments with ligands **7a** and **9** endothermic heat effects were observed, indicating deaggregation of the ligand upon dilution. The binding constants (K) and ΔH values for ligand : metal complexation were corrected by compensating K and ΔH for dilution and deaggregation when applicable in the plots of ΔH *versus* molar ratio.

From Table 1 it is clear that the central oxygen atom containing ligands **4a** and **4b** show a complexation affinity

Table 1 Binding constants and thermodynamic parameters of the binding of ligands **4a,b, 7a,b, 9, 13**, and **25** with Eu(III) determined with microcalorimetry in acetonitrile at 30 °C[a]

Ligand	K, L mol^{-1}	$\Delta G°$, kJ mol^{-1}	$\Delta H°$, kJ mol^{-1}	$T\Delta S°$, kJ mol^{-1}
4a	2.5×10^4	−25.1	−4.2	20.9
4b	4.7×10^5	−32.2	−2.5	29.7
7a[b]	4.4×10^5	−32.2	−33.1	−0.9
	1.8×10^4	−25.5	−20.1	5.4
7b[b]	2.3×10^5	−30.6	−40.6	−10.0
	5.7×10^4	−27.2	−87.5	−60.3
9	2.0×10^4	−24.7	−6.3	18.4
13	3.3×10^4	−25.5	−81.2	−55.7
25[b]	7.6×10^4	−28.0	−20.1	7.9
	5.8×10^4	−27.2	−2.9	24.3

[a] Ligand conc. (burette) = 2 mmol L^{-1}, Eu(III) conc. (cell) = 0.066 mmol L^{-1}; in the case of **4a,b** the concentrations are halved. [b] Data showed the best fit for 2 : 1 (L : M) complexation, so the thermodynamic parameters are given for both the 1 : 1 (first row) and 2 : 1 (second row) complexes.

towards Eu(III) with **4b** having a slightly higher stability constant than **4a** and a sufficiently good fit for 1 : 1 (ligand : metal) complexation. The order is in line with the extraction data obtained at low HNO_3 concentration (Fig. 1). For ligand **4a** the binding enthalpy is less exothermic than that of **4b**, however, **4b** has a higher positive entropy compared to **4a** showing the stronger release of solvent molecules from the coordination sphere.

The ligands **7a** and **7b** show a complexation affinity towards Eu(III) in a comparable order with a sufficiently good fit for 2 : 1 (ligand : metal) complexation. For ligand **7a** the first binding enthalpy is exothermic as expected with a slightly negative entropy. However, the second binding enthalpy is less exothermic, which in turn is compensated by the positive entropy owing to the release of solvent molecules from the coordination sphere. Ligand **7b** shows a comparable exothermic binding enthalpy with a slightly negative entropy. However, it exhibits a stronger exothermic binding enthalpy for the second ligand binding, which is compensated by a large negative entropy.

The tripodal ligand **9**, with two dioctylamide moieties and one dibutyl phosphonate, also shows the best fit for 1 : 1 (ligand : metal) complexation, in an exothermic process. It has a binding affinity for Eu(III) with a negative binding enthalpy, however, the more positive entropy indicates the release of solvent molecules from the coordination sphere. Ligand **13**, with two butylphosphonate and one dioctylamide group, shows a stronger binding efficiency than **9**, also showing the best fit for 1 : 1 (ligand : metal) complexation, which clearly corresponds with the extraction data (Fig. 3). This can be partly attributed to the presence of two sterically hindering dioctyl groups and partly to the presence of two butyl phosphonate groups that act as stronger donors than the amide moieties. Ligand **13** shows a high exothermic enthalpy and a high negative entropy of binding. These ligands did also not show good extraction efficiencies due to the protonation of the central nitrogen atom under the highly acidic extraction conditions.

Ligand **25** shows a good fit for 2 : 1 (ligand : metal) complexation with a first negative binding enthalpy and positive entropy. In the second binding step the ligand exhibits a less negative enthalpy, which is compensated by a larger positive entropy indicating the release of solvent molecules from the coordination sphere. It shows the highest extraction efficiency compared to all other ligands (Fig. 5). This is not reflected in the *K* values in Table 1. It should be kept in mind, however, that these cannot be directly compared, since the microcalorimetric experiments could not be carried out under similar conditions as the extractions were done due to solubility reasons.

Conclusions

Different types of hybrid-like ligands were successfully prepared in which essential parts of well-known ligands were combined. Interestingly, the mixed type ligand **4a** shows a steeper acid dependency than CMPO, which makes the development of a partitioning process much easier, since the stripping of the actinides from a loaded phase is more facile. Surprisingly, the diphosphonothioate-based malonamide analogue **25** exhibited a much better extraction efficiency than the regular malonamides. For the ligands studied, the extraction trend was clearly demonstrated by microcalorimetry.

Experimental

General

All moisture-sensitive reactions were carried out under an argon atmosphere. The solvents and all reagents were obtained from commercial sources and used without further purification. All known compounds *viz*. **2a**,[23] **3**,[24] **5a,b**,[28] **8**,[24] **14**[29] and **24**[30] were prepared according to literature procedures. Solvents were dried according to standard procedures and stored over molecular sieves. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Unity INOVA (300 MHz) spectrometer. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) chemical shift values are reported as δ using the residual solvent signal as an internal standard. Electrospray ionization (positive mode) mass spectra and high resolution mass spectra were recorded on a WATERS LCT mass spectrometer. Elemental analyses were performed using a Flash 200 CHN analyzer of Thermo Scientific/Interscience. Analytical TLC was performed using Merck prepared plates (silica gel 60 F-254 on aluminum). Column chromatography was carried out on Merck silica gel 60 (230–400 mesh).

Di-*n*-butyl(hydroxymethyl)phosphinoxide (2b)

A mixture of **1b** (0.81 g, 5.0 mmol), K_2CO_3 (0.04 g, 0.3 mmol), and paraformaldehyde (0.18 g, 6 mmol) in cyclohexane (15 mL) was stirred at room temperature for 48 h. The mixture was filtered and concentrated under reduced pressure to give **2b** in quantitative yield. ^{1}H NMR δ: 0.92 (6H, t, J = 7.4 Hz, CH_3), 1.31–1.44 (4H, m, CH_2CH_3), 1.48–1.60 (4H, m, PCH_2CH_2), 1.65–1.79 (4H, m, PCH_2), 3.87 (2H, d, J = 6.4 Hz, PCH_2O). MS: m/z 193.1 $[M + H]^+$. $C_9H_{22}O_2P$ calculated 193.2.

Di-*n*-butyl((2-(di-*n*-octylamino)-2-oxoethoxy)methyl)-phosphonate (4a)

A suspension of **2a** (0.69 g, 3.1 mmol), (NaH 60%) in oil (0.15 g, 3.5 mmol), and KI (0.52 g, 3.1 mmol) in dry THF (25 mL) was stirred for 1 h at 0 °C. A solution of 2-chloro-*N*,*N*-dioctylacetamide (**3**) (1.00 g, 3.5 mmol) in THF (25 mL) was added dropwise to the mixture over 20 min at 0 °C followed by stirring at room temperature for 3 h. The reaction mixture was quenched with saturated NH_4Cl solution (10 mL). The solvent was evaporated and the residue was dissolved in ethyl acetate (30 mL). The resulting solution was washed with water (3 × 25 mL). The organic layer was dried with anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was separated by chromatography (SiO_2, ethyl acetate : methanol, 95 : 5) to afford **4a** (0.98 g, 63%) as an oil. ^{1}H NMR δ: 0.80–1.01 (12H, m, CH_3), 1.20–1.30 (20H, s, $(CH_2)_5CH_3$), 1.39 (4H, sextet, J = 7.0 Hz, CH_2CH_3), 1.52 (4H, s, NCH_2CH_2), 1.66 (4H, pentet, J = 7.0 Hz, OCH_2CH_2), 3.07, 3.20 (2H, t, J = 6.4 Hz, CH_2N), 3.95 (2H, d, J = 7.7 Hz, PCH_2O), 4.03–4.17 (4H, m, $POCH_2$), 4.29 (2H, s, $C(O)CH_2O$). ^{13}C NMR δ: 14.0, 18.5, 27.0, 29.3, 31.8, 49.6, 67.0, 69.0, 166.5. HRMS: m/z 506.3988 $[M + H]^+$. $C_{27}H_{57}NO_5P$ calculated 506.3974.

2-((Di-*n*-butylphosphoryl)methoxy)-*N*,*N*-di-*n*-octylacetamide (4b)

By the same procedure as described for **4a**, starting from **2b** (0.60 g, 3.1 mmol), NaH (60% in oil) (0.15 g, 3.5 mmol), KI (0.52 g, 3.1 mmol), and **3** (0.98 g, 3.1 mmol) afforded **4b** (1.07 g, 73% yield) as an oil. ^{1}H NMR δ: 0.81–1.01 (12H, m, CH_3), 1.18–1.26 (20H, m, $(CH_2)_5CH_3$), 1.34–1.62 (12H, m, $CH_2CH_2CH_3$, NCH_2CH_2), 1.64–1.80 (4H, m, PCH_2CH_2), 3.05, 3.22 (2H, t, J = 6.4 Hz, CH_2N), 3.83 (2H, d, J = 6.4 Hz, PCH_2O), 4.17 (2H, s, $COCH_2O$). ^{13}C NMR δ: 14.0, 22.7, 24.7, 27.0, 29.3, 31.8, 49.6, 69.0, 166.5. HRMS: m/z 474.4099 $[M + H]^+$. $C_{27}H_{57}NO_3P$ calculated 474.4076.

Di-*n*-butyl((benzyl(2-(di-*n*-octylamino)-2-oxoethyl)amino)methyl)-phosphonate (6a).

A mixture of **5a** (1.00 g, 3.0 mmol), **3** (1.11 g, 3.3 mmol), KI (0.47 g, 3 mmol) and K_2CO_3 (1.32 g, 9.5 mmol) in acetonitrile (50 mL) was refluxed for 48 h. The solvent was evaporated and the residue was dissolved in dichloromethane (200 mL). The resulting solution was washed with water (3 × 50 ml). The organic layer was dried with anhydrous $MgSO_4$ and concentrated under reduced pressure, followed by purification by chromatography (SiO_2, ethyl acetate) to give **6a** (1.28 g, 62% yield) as an oil. ^{1}H NMR δ: 0.82–0.95 (12H, m, CH_3), 1.20–1.30 (20H, m, $(CH_2)_5CH_3$), 1.39 (4H, sextet, J = 7.0 Hz, CH_2CH_3), 1.42–1.46 (4H, m, NCH_2CH_2), 1.63 (4H, pentet, J = 7.0 Hz, OCH_2CH_2), 3.05, 3.25 (2H, t, J = 6.5 Hz, $CONCH_2$), 3.21 (2H, d, J = 9.9 Hz, PCH_2N), 3.53 (2H, s, NCH_2Ar), 3.92–4.07 (4H, m, $POCH_2$), 3.81 (2H, s, $C(O)CH_2N$), 7.21–7.39 (5H, m, ArH). MS: m/z 595.7 $[M + H]^+$. $C_{34}H_{64}N_2O_4P$ calculated 595.5.

2-(Benzyl((di-*n*-butylphosphoryl)methyl)amino)-*N*,*N*-di-*n*-octylacetamide (6b)

Using the same procedure as described for **6a**, starting from **5b** (0.89 g, 3.0 mmol), **3** (1.11 g, 3.3 mmol), KI (0.47 g, 3 mmol), and K_2CO_3 (1.32 g, 9.5 mmol) gave **6b** as an oil (1.42 g, 73% yield). ^{1}H NMR δ: 0.82–0.95 (12H, m, CH_3), 1.15–1.23 (20H, m, $(CH_2)_5CH_3$), 1.30–1.60 (12 H, m, NCH_2CH_2, $PCH_2(CH_2)_2$), 1.60–1.74 (4H, m, PCH_2), 3.05, 3.25 (2H, t, J = 6.5 Hz, $CONCH_2$), 3.06 (2H, d, J = 4.7 Hz, PCH_2N), 3.60 (2H, s, NCH_2Ar), 3.94 (2H, s, $C(O)CH_2N$), 7.25–7.51 (5H, m, ArH). MS: m/z 563.4 $[M + H]^+$. $C_{34}H_{64}N_2O_2P$ calculated 563.5.

Di-*n*-butyl(((2-(di-*n*-octylamino)-2-oxoethyl)amino)methyl)-phosphonate (7a)

A suspension of **6a** (1.00 g, 1.7 mmol) and 5% Pd/C (300 mg) in ethanol (50 mL) was stirred under a hydrogen atmosphere overnight. The catalyst was filtered off and the ethanol was removed under reduced pressure to give **7a** as an oil in quantitative yield. ^{1}H NMR δ: 0.90–0.95 (12H, m, CH_3), 1.24–1.30 (20H, m, $(CH_2)_5CH_3$), 1.39 (4H, sextet, J = 7.0 Hz, CH_3CH_2), 1.50–1.54 (4H, m, NCH_2CH_2), 1.66 (4H, pentet, J = 7.0 Hz, $POCH_2CH_2$), 3.15, 3.30 (2H, t, J = 6.5 Hz, $CONCH_2$), 3.03 (2H, d, J = 11.9 Hz, PCH_2N), 3.52 (2H, s, $COCH_2N$), 4.06–4.15 (4H, m, $POCH_2$). ^{13}C NMR δ: 14.0, 18.5, 22.7, 24.0, 24.4, 27.0, 29.3, 31.8, 50.0, 66.9, 164.0. HRMS: m/z 505.4119 $[M + H]^+$. $C_{27}H_{57}N_2O_4P$ calculated 505.4134.

2-(((Di-*n*-butylphosphoryl)methyl)amino)-*N*,*N*-di-*n*-octylacetamide (7b)

It was synthesized by the same procedure as described for **7a**, starting from **6b** (1.20 g, 2.1 mmol) and 5% Pd/C (300 mg) in ethanol (50 mL) in quantitative yield. ^{1}H NMR δ: 0.85–0.95 (12H, m, CH_3), 1.20–1.28 (20H, m, $(CH_2)_5CH_3$), 1.26–1.65 (12 H, m, NCH_2CH_2, $(PCH_2(CH_2)_2)$, 1.65–1.78 (4H, m, PCH_2), 3.00 (2H, d, J = 7.9 Hz, PCH_2N), 3.04, 3.21 (2H, t, J = 6.6 Hz, $CONCH_2$), 3.54 (2H, s, $COCH_2N$). ^{13}C NMR δ: 14.0, 22.7, 24.0, 24.4, 27.0, 29.3, 31.3, 49.0, 52.6, 164.0. HRMS: m/z 473.4229 $[M + H]^+$. $C_{27}H_{58}N_2O_2P$ calculated 473.4236.

Di-*n*-butyl((bis(2-(di-*n*-octylamino)-2-oxoethyl)amino)methyl)-phosphonate (9)

A mixture of **8** (0.80 g, 1.5 mmol), paraformaldehyde (0.05 g, 1.6 mmol), **1a** (0.31 g, 1.6 mmol), *p*-toluenesulfonic acid (0.10 g), and molecular sieves in toluene (35 mL) was refluxed for 48 h. Subsequently, K_2CO_3 (0.50 g) was added and the mixture was refluxed for 10 min. After cooling to room temperature, the mixture was washed with water (1 × 20 mL), dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography (SiO_2, ethyl acetate) to afford **9** (0.65 g, 60%) as an oil. ^{1}H NMR δ: 0.82–0.94 (18H, m, CH_3), 1.23–1.30 (40H, s, $(CH_2)_5CH_3$), 1.38 (4H, sextet, J = 7.0 Hz, CH_3CH_2), 1.43–1.47 (8H, m, NCH_2CH_2), 1.62 (4H, pentet, J = 7.0 Hz, OCH_2CH_2), 3.17, 3.23 (4H, t, J = 6.6 Hz, $CONCH_2$), 3.31 (2H, d, J = 9.3 Hz, PCH_2N), 3.74 (4H, s, NCH_2CO), 4.07 (4H, q, J = 7.0 Hz, CH_2OP), ^{13}C NMR δ: 14.0, 18.5, 22.7, 27.0, 29.3, 31.8, 49.3, 60.0, 60.5, 66.9, 167.5. HRMS: m/z 786.6879 $[M + H]^+$. $C_{45}H_{93}N_3O_5P$ calculated 786.6853.

Tetra-*n*-butyl((benzylazanediyl)bis(methylene))-bis(phosphonate) (11)

A mixture of benzylamine (**10**) (0.43 g, 4.0 mmol), paraformaldehyde (0.24 g, 8.0 mmol), **1a** (1.79 g, 8.0 mmol), *p*-toluenesulfonic acid (0.11 g), and molecular sieves in toluene (35 mL) was refluxed for 24 h. Subsequently, K_2CO_3 (0.50 g) was added and the mixture was refluxed for 10 min. The mixture was washed with water (1 × 20 mL), dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography (SiO_2, ethyl acetate) to give **11** (1.49 g, 72%) as an oil. ^{1}H NMR δ: 0.85–0.96 (12H, m, CH_3), 1.37 (8H, sextet, J = 7.0 Hz, CH_2CH_3), 1.62 (8H, pentet, J = 7.0 Hz, OCH_2CH_2), 3.16 (4H, d, J = 9.2 Hz, PCH_2N), 3.94–4.09 (8H, m, $POCH_2$), 4.02 (2H, s, $ArCH_2N$), 7.22–7.40 (5H, m, ArH). MS: m/z 520.3 $[M + H]^+$. $C_{25}H_{48}NO_6P_2$ calculated 520.3.

Tetra-*n*-butyl(azanediylbis(methylene))bis(phosphonate) (12)

A suspension of **11** (1.30 g, 2.5 mmol) and 10% Pd/C (300 mg) in ethanol (50 mL) was stirred under a hydrogen atmosphere (10 bar) at room temperature for 72 h. The catalyst was filtered off and the solvent was removed under reduced pressure, to give **12** as an oil in quantitative yield. ^{1}H NMR δ: 0.82–0.97 (12H, m, CH_3), 1.37 (8H, sextet, J = 7.0 Hz, CH_2CH_3), 1.63 (8H, pentet, J = 7.0 Hz, OCH_2CH_2), 3.11 (4H, d, J = 10.6 Hz, PCH_2N),

4.02–4.14 (8H, m, $POCH_2$). MS: m/z 430.3 $[M + H]^+$. $C_{18}H_{42}NO_6P_2$ calculated 430.2.

Tetra-*n*-butyl(((2-(di-*n*-octylamino)-2-oxoethyl)azanediyl)-bis(methylene))bis(phosphonate) (13)

A mixture of **3** (0.60 g, 1.9 mmol), **12** (0.77 g, 1.8 mmol), K_2CO_3 (0.74 g, 5.4 mmol), and KI (0.27 g, 1.8 mmol) in acetonitrile (50 mL) was refluxed for 48 h. The solvent was evaporated and the residue was dissolved in dichloromethane (200 mL). The resulting solution was washed with water (3 × 50 mL). The organic layer was dried with anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by chromatography (SiO_2, dichloromethane : methanol, 97 : 3) to give **13** (1.04 g, 78% yield) as an oil. ^{1}H NMR δ: 0.82–0.96 (18H, m, CH_3), 1.23–1.29 (20H, m, $(CH_2)_5CH_3$), 1.38 (8H, sextet, J = 7.0 Hz, CH_2CH_3), 1.49–1.53 (4H, m, NCH_2CH_2), 1.63 (8H, pentet, J = 7.0 Hz, OCH_2CH_2), 3.16, 3.23 (2H, t, J = 6.6 Hz, $CONCH_2$), 3.35 (4H, d, J = 9.3 Hz, PCH_2N), 3.84 (2H, s, $NCH_2C(O)$), 4.06–4.15 (8H, m, CH_2OP). ^{13}C NMR δ: 14.0, 18.5, 22.7, 27.0, 29.3, 31.8, 49.3, 58.2, 66.9, 167.5. HRMS: m/z 711.5194 $[M + H]^+$. $C_{36}H_{77}N_2O_7P_2$ calculated 711.5206.

Tetra-*n*-butyl(oxybis(methylene))bis(phosphonate) (15)

To a solution of **2a** (1.00 g, 4.4 mmol) in THF (40 mL) was slowly added NaH (60% in oil) (0.2 g, 5 mmol) portionwise at 0 °C. After stirring at this temperature for 1 h, a solution of (di-*n*-butoxyphosphoryl)methyl trifluoromethanesulfonate (**14**) (1.58 g, 4.4 mmol) in THF (15 mL) was added and stirring was continued overnight at room temperature. The solvent was evaporated and the residue was dissolved in chloroform (30 mL). The resulting solution was washed with 10% HCl (3 × 50 mL) and water (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure, followed by purification of the residue with chromatography (SiO_2, dichloromethane) to afford **15** (1.29 g, 68%) as an oil. ^{1}H NMR δ: 0.95 (12H, t, J = 7.0 Hz, CH_3), 1.39 (8H, sextet, J = 7.0 Hz, CH_3CH_2), 1.63 (8H, pentet, J = 7.0 Hz, OCH_2CH_2), 3.84 (4H, d, J = 7.5 Hz, OCH_2P), 4.10 (8H, pentet, J = 7.0 Hz, OCH_2). ^{13}C NMR δ: 13.8, 18.9, 32.6, 66.9, 72.5, 74.2. HRMS m/z 431.2339 $[M + H]^+$. $C_{18}H_{41}O_7P_2$ calculated 431.2328.

***O,O,O′,O′*-Tetra-*n*-butyl(oxybis(methylene))-diphosphonothioate (16)**

A solution of **15** (1.00 g, 2.3 mmol) and Lawesson's reagent (1.88 g, 4.6 mmol) was refluxed in toluene for 2 h. After removal of the solvent the residue was separated by chromatography (SiO_2, dichloromethane) to afford **16** (0.85 g, 80%) as an oil. ^{1}H NMR δ: 0.95 (12H, t, J = 7.0 Hz, CH_3), 1.39 (8H, sextet, J = 7.0 Hz, CH_2CH_3), 1.63 (8H, pentet, J = 7.0 Hz, OCH_2CH_2), 4.18 (4H, d, J = 7.5 Hz, OCH_2P), 4.07 (8H, pentet, J = 7.0 Hz, OCH_2). ^{13}C NMR δ: 13.8, 18.9, 32.6, 66.9, 72.3, 74.1. HRMS: m/z 463.1893 $[M + H]^+$. $C_{18}H_{41}O_5P_2S_2$ calculated 463.1871.

(Hydroxymethyl)diphenylphosphine sulfide (18)

A mixture of **17** (1.00 g, 4.6 mmol), paraformaldehyde (0.15 g, 5.0 mmol), and K_2CO_3 (0.07 g, 0.5 mmol) in ethanol (15 mL) was refluxed for 4 h. The mixture was cooled to room temperature, filtered and the solvent was evaporated under reduced pressure to afford **18** in quantitative yield. ^{1}H NMR δ: 3.03 (1H, bs, OH), 4.42 (2H, s, CH_2), 7.43–7.61 (6H, m, ArH), 7.70–7.83 (4H, m, ArH). MS: m/z 248.2 $[M + H]^+$. $C_{13}H_{13}OPS$ calculated 248.0.

(Oxybis(methylene))bis(diphenylphosphine sulfide) (20)

To a solution of **18** (1.00 g, 4.0 mmol) in dichloromethane (50 mL), containing triethylamine (0.50 g, 4.9 mmol) as a base, was added *p*-toluenesulfonyl chloride (0.76 g, 4 mmol). The resulting mixture was stirred overnight at room temperature, washed with water (3 × 50 mL), and the solvent was removed under reduced pressure to afford tosylate **19** (1.25 g, 78%). ^{1}H NMR δ: 4.62 (4H, d, J = 6.0 Hz, OCH_2P), 7.27 (2H, d, J = 7.5 Hz, ArH), 7.42–7.52 (4H, m, ArH), 7.53–7.62 (4H, m, ArH), 7.72–7.83 (4H, m, ArH). To a solution of **18** (1.00 g, 4.0 mmol) in THF (50 mL) was added NaH (60% in oil) (0.20 g, 5.0 mmol) at 0 °C. After stirring at this temperature for 1 h, a solution of **19** (1.61 g, 4 mmol) in THF (10 mL) was added dropwise at 0 °C. The resulting mixture was stirred at room temperature overnight. The solvent was evaporated and the residue was dissolved in dichloromethane (50 mL), washed with 10% HCl (2 × 50 mL) and water (2 × 50 mL). The organic layer was concentrated under reduced pressure and the residue was purified by chromatography (SiO_2, dichloromethane : methanol, 97 : 3) to afford **20** (0.84 g, 71%) as a solid. (found C, 65.16; H, 5.11. $C_{26}H_{24}OP_2S_2$ requires C, 65.26; H, 5.06%). m.p. 104–106 °C. ^{1}H NMR δ: 4.42 (4H, d, J = 6.0 Hz, OCH_2P), 7.33–7.42 (8H, m, ArH), 7.48–7.56 (4H, m, ArH), 7.65–7.75 (8H, m, ArH). ^{13}C NMR δ: 75.5, 76.3, 128.7, 129.9, 131.0, 132.2. MS: m/z 479.1 $[M + H]^+$. $C_{26}H_{25}OP_2S_2$ calculated 479.1.

(Oxybis(methylene))bis(di-*n*-butylphosphinoxide) (22)

To a solution of **2b** (1.50 g, 7.8 mmol) in dichloromethane (50 mL), containing triethylamine as a base (0.81 g, 8.0 mmol), was added *p*-toluenesulfonyl chloride (1.48 g, 7.8 mmol). The resulting mixture was stirred overnight at room temperature, washed with water (3 × 50 mL), and the solvent was removed under reduced pressure to afford (dibutylphosphoryl)methyl 4-methylbenzenesulfonate **21** (1.85 g, 65%). ^{1}H NMR δ: 0.89 (6H, t, J = 7.5 Hz, CH_3), 1.32–1.48 (4H, m, CH_3CH_2), 1.50–1.64 (4H, m, PCH_2CH_2), 1.66–1.83 (4H, m, PCH_2)), 4.15 (2H, d, J = 7.5 Hz, OCH_2P), 7.39 (2H, d, J = 8.1 Hz, ArH), 7.80 (2H, d, J = 8.1 Hz, ArH). To a solution of **2b** (1.00 g, 5.2 mmol) in THF (50 mL) was added NaH (60% in oil) (0.24 g, 6.0 mmol) at 0 °C. After stirring at this temperature for 1 h, a solution of **21** (1.80 g, 5.2 mmol) in THF (10 mL) was added dropwise at 0 °C. The resulting mixture was stirred at room temperature overnight. The solvent was evaporated and the residue was dissolved in dichloromethane (50 mL), washed with 10% HCl (2 × 50 mL) and water (2 × 50 mL). The organic layer was concentrated under reduced pressure and the residue was purified by chromatography (SiO_2, dichloromethane) to give **22** (0.80 g, 76%) as an oil. ^{1}H NMR δ: 0.94 (12H, t, J = 7.2 Hz, CH_3), 1.42 (8H, sextet, J = 7.2 Hz, CH_3CH_2), 1.51–1.67 (8H, m, PCH_2CH_2), 1.67–1.84

(8H, m, PCH_2), 3.88 (4H, d, J = 6.0 Hz, OCH_2P). ^{13}C NMR δ: 13.9, 24.1, 28.7, 29.3, 71.6, 72.9. HRMS: m/z 367.2549 $[M + H]^+$. $C_{18}H_{41}O_3P_2$ calculated 367.2531.

(Oxybis(methylene))bis(di-*n*-butylphosphine sulfide) (23)

A solution of **22** (0.80 g, 2.2 mmol) and Lawesson's reagent (1.76 g, 4.4 mmol) was refluxed in toluene for 2 h. After removal of the solvent the residue was separated by chromatography (SiO_2, dichloromethane) to afford **23** (0.68 g, 80%) as a solid (found C, 54.22; H, 10.07. $C_{18}H_{40}OP_2S_2$ requires C, 54.24; H, 10.12%). m.p. 81–83 °C. ^1H NMR δ: 0.95 (12H, t, J = 7.5 Hz, CH_3), 1.44 (8H, sextet, J = 6.0 Hz, CH_3CH_2), 1.53–1.96 (16H, m, PCH_2CH_2), 3.91 (4H, d, J = 6.0 Hz, OCH_2P). ^{13}C NMR δ: 13.9, 24.1, 28.5, 29.1, 71.8, 72.6. MS: m/z 399.3 $[M + H]^+$. $C_{18}H_{41}OP_2S_2$ calculated 399.2.

O,*O*,*O*′,*O*′-Tetra-*n*-butyl methylenediphosphonothioate (25)

To a solution of methylenediphosphonothioic dichloride **24** (1.00 g, 3.5 mmol) and 1*H*-tetrazole (0.04 g, 0.6 mmol) in toluene (50 mL) was added dropwise a solution of 1-butanol (1.05 g, 14.0 mmol) and diisopropylethylamine (2.27 g, 17.6 mmol) in toluene (20 mL) over a 2 h period. After stirring overnight at room temperature, the diisopropylethylammonium and tetrazonium salts were removed by filtration. Upon evaporation of the solvent the product was purified by chromatography (SiO_2, dichloromethane) to afford tetraester **25** (1.35 g, 90%) as an oil. ^1H NMR δ: 0.93 (12H, t, J = 7.5 Hz, CH_3), 1.40 (8H, sextet, J = 7.5 Hz, CH_3CH_2), 1.64 (8H, pentet, J = 7.5 Hz, OCH_2CH_2), 2.99 (2H, t, J = 18.0 Hz, PCH_2P), 3.98–4.18 (8H, m, OCH_2). ^{13}C NMR δ: 13.9, 19.0, 32.4, 42.3, 67.1. HRMS: m/z 433.1778 $[M + H]^+$. $C_{17}H_{39}O_4P_2S_2$ calculated 433.1765.

Methylenebis(di-*n*-butylphosphine sulfide) (26)

To a solution of **24** (1.00 g, 3.5 mmol) in THF (50 mL), a solution of *n*-butylmagnesium chloride (2 M in THF) (7.5 mL, 15.0 mmol) was added dropwise over a period of half an hour at −78 °C. The resulting mixture was brought to room temperature in 2 h, followed by overnight stirring at room temperature. The solvent was evaporated and the residue was dissolved in dichloromethane (50 mL). The resulting solution was washed with 10% HCl (2 × 30 mL), water (2 × 30 mL), and brine (2 × 30 mL). The organic layer was concentrated under reduced pressure and the crude product was purified by chromatography (SiO_2, dichloromethane) to afford **26** (0.85 g, 66%) as a colorless oil. ^1H NMR δ: 0.95 (12H, t, J = 7.5 Hz, CH_3), 1.46 (8H, sextet, J = 7.5 Hz, CH_3CH_2), 1.54–1.67 (8H, m, PCH_2CH_2), 2.07–2.21 (8H, m, PCH_2), 2.46 (2H, t, J = 12.0 Hz, PCH_2P). ^{13}C NMR δ: 13.9, 24.0, 24.7, 31.8, 32.8, 33.6. ES^+ MS: m/z 369.1993 $[M + H]^+$. $C_{17}H_{39}P_2S_2$ calculated 369.1968.

Microcalorimetry

Calorimetric measurements were carried out in acetonitrile using a Microcal VP-ITC microcalorimeter with a cell volume of 1.4115 mL. For studying the complexation of Eu(III) to the ligands **7a,b**, **9**, **13**, and **25**, aliquots of a 2.0 mmol L^{-1} solution (10 μL) of the ligands (1.0 mmol L^{-1} for ligands **4a,b**) in the burette were added to a 0.066 mmol L^{-1} solution (0.033 mmol L^{-1} for ligands **4a,b**) of Eu(III) perchlorate in the calorimetric cell, monitoring the heat change after each addition.

Extraction procedure

All the lipophilic ligands were dissolved in TPH (hydrogenated tetrapropene) at a preferable concentration of 0.1 mol L^{-1}. Complete dissolution of ligands **20** and **25** was only obtained by decreasing their concentration or addition of 1-octanol. The obtained organic solvent was contacted with nitric acid of variable concentrations (0.01–5 mol L^{-1}) containing traces of Am(III) and Eu(III). Nitric acid solutions were prepared by diluting concentrated nitric acid (Merck KGa, Darmstadt, Germany) with ultrapure water (resistivity, 18 MΩcm). Their acidity was checked by titration with NaOH.

The batch extraction experiments were performed in 2 mL glass vials. Organic and aqueous phases (500 μL) were spiked with 10 μL of radiotracer (^{241}Am, ^{152}Eu, approx. 25 kBq mL^{-1}) and shaken by a vortex mixer for 60 min at 22 ± 1 °C using an IKA Vibrax Orbital Shaker Model VXR (2200 rpm). Experiments using CMPO were conducted with 15 min phase contact time, which is enough to reach equilibrium. Separation of the phases by centrifugation was followed by sampling of 200 μL of each phase for analysis using a high-purity germanium spectrometer system purchased from EG&G Ortec, München, Germany, and equipped with the gamma vision software. The γ-lines at 59.5 and 121.8 keV were examined for ^{241}Am and ^{152}Eu, respectively. The distribution ratio D was measured as the ratio between the radioactivity of an isotope in the organic and the aqueous phase. Distribution ratios between 0.1 and 100 exhibit a maximum error of ±5%. The error may be up to ±20% for smaller and larger values.

The kinetics extraction experiments were performed similarly as described above, except the phases contact time (mixing time).

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