Metal Complexation by Tripodal *N*-Acyl(thio)urea and Picolin(thio)amide Compounds: Synthesis/Extraction and Potentiometric Studies

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The synthesis and binding properties towards different cations of a series of tripodal ligands functionalized with *N*-acyl(thio)urea and picolin(thio)amide moieties are described. For the extraction of Am^{3+} and Eu^{3+} the compounds are not efficient. However, *N*-acylurea derivative **10** exhibit a significant selectivity for Am^{3+} over Eu^{3+}. Upon addition of the synergistic hexabrominated bis(dicarbollide)cobalt anion (Br_6-COSAN) the distribution coefficients for Am^{3+} and Eu^{3+} increase up to 1000 for picolinamide derivative **11**. Extraction studies with metal picrates (Pb^{2+}, Cu^{2+}, Ag^{+}, Hg^{2+}, Cd^{2+}, Eu^{3+}, Fe^{3+}, K^{+}, Na^{+}, and Ca^{2+}) or the incorporation in ion selective electrodes (ISEs), show that picolinamide derivative **11** is a very selective and strong ionophore for Hg^{2+} and that *N*-acylthiourea **8** is a very good ionophore for Ag^{+}.

Introduction

The separation of actinides from lanthanides is an important problem in nuclear waste treatment.[1] They are very similar, but most radioactive lanthanide isotopes are much shorter living. In addition, lanthanides tend to absorb neutrons efficiently, preventing the effective transmutation of americium and curium present in the nuclear waste mixture.[2]

Actinides have a higher coordinative character than lanthanides, and therefore the separation of actinides from lanthanides is favored by the presence of softer donor atoms than oxygen such as sulfur or phosphorus.[3] Over the years different types of ligands have been used for actinide/lanthanide separation as there are carbamoylmethyl phosphane oxide (CMPO),[4] Cyanex,[5] malonamides,[6] diglycolamides,[7] pyrazolones,[8] bis(triazinyl)pyridines,[9] etc. It has been demonstrated that attachment of four CMPO or picolinamide moieties to a calix[4]arene[10] or cavitand[11] platform gives rise to higher extraction efficiencies and selectivities than the individual ligands.

In the case of CMPO ligating sites, a 3:1 stoichiometry is needed to extract americium cations from the acidic nuclear waste.[12] This implies that a C_3-symmetrical platform would be suitable. For other applications the C_3-symmetrical cyclotriveratrylenes (CTV)[13] and 1,3,5-trisubstituted 2,4,6-triethylbenzenes[14] are being used as a scaffold.

Recently, it has been reported that connection of three 2-pyridylmethyl or 2-pyrazinylmethyl moieties to a nitrogen gives ionophores that selectively extract actinides in the presence of lanthanides.[15]

The attachment of three CMPO moieties to a rigid C_3-symmetric triphenoxymethane platform gave an ionophore **1** with enhanced selectivity for Th^{4+} over lanthanides.[16] Shanzer and co-workers used tripodal structures of type **2** with flexible arms, based on trimethylolpropane, for the complexation of Ca^{2+}.[17] The commercially available Na^{+} ionophore **3** is based on the same skeleton (Scheme 1).[18]

In this paper the synthesis, extraction, and sensing behavior of trimethylolpropane-based tripodal ionophores with picolin(thio)amide and *N*-acyl(thio)urea ligating sites will be discussed (Scheme 2). The results with the corresponding CMP(O) derivatives will be reported in a forthcoming paper. Picolinamide moieties were selected because of their soft donor character and their selectivity towards actinides over lanthanides.[19–21] *N*-acylthiourea moieties were selected as potential ligating groups for actinide/lanthanide complexation because of the presence of sulfur, nitrogen, and oxygen as donor atoms. The soft donor character of *N*-acylthioureas makes them possible candidates for actinide/lanthanide complexation. To investigate the possible wider applicability of the tripodal ionophores **7**–**12**, their behavior towards a variety of other cations has also been studied.

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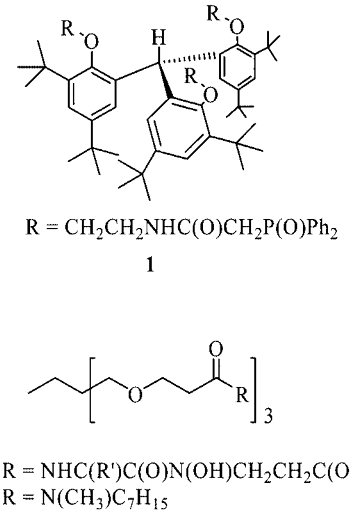
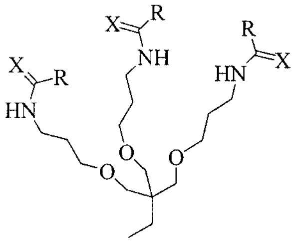


R = $CH_2CH_2NHC(O)CH_2P(O)Ph_2$

1

2 R = $NHC(R')C(O)N(OH)CH_2CH_2C(O)OH$
3 R = $N(CH_3)C_7H_{15}$

Scheme 1.



	X	R
7	S	NHC(O)Ph
8	S	NHC(O)OEt
9	O	NHC(O)Ph
10	O	NHC(O)OEt
11	O	Py
12	S	Py

Scheme 2.

Results and Discussion

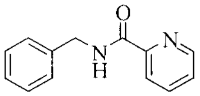
Synthesis

The synthesis of the C_3-symmetric tripodal ligands **7**–**12** is summarized in Scheme 3. The known reaction of trimethylolpropane (**4**) with acrylonitrile, using KOH as a base, afforded the Michael adduct **5** as a yellow oil in 81% yield.[17] Catalytic hydrogenation of **5** with Raney-Co gave 1,1,1-tris[(aminopropoxy)methyl]propane (**6**) in 83% yield. A new signal at 1.63–1.70 ppm of three CH_2 groups in the ^1H NMR spectrum indicated its formation.

Subsequent reaction of **7** with the appropriate iso(thio)cyanates in acetonitrile gave compounds **7**, **8**, **9**, and **10** in 97%, 75%, 96%, and 74% yield, respectively. In all cases the introduction of the acyl(thio)urea groups induced in the ^1H NMR spectra a downfield shift for the methylene protons next to the chelating group, from 2.80 in **7** to 3.79 and 3.78 ppm for the acylthioureas **7** and **8**, and to 3.41–3.51 and 3.40 ppm for the acylureas **9** and **10**, respectively.

Picolinamido derivative **11** was obtained in 50% yield by reaction of **6** with pentafluorophenyl picolinate in dry THF. The downfield shift in the ^1H NMR spectrum of the methylene protons adjacent to the picolinamide from 2.80 in **7** to 3.60 ppm confirmed its formation. Subsequent reaction of **11** with Lawesson's reagent in refluxing toluene afforded picolinthioamide derivative **12** in 37% yield.

Model compound **13** (Scheme 4) was synthesized following a literature procedure.[22]



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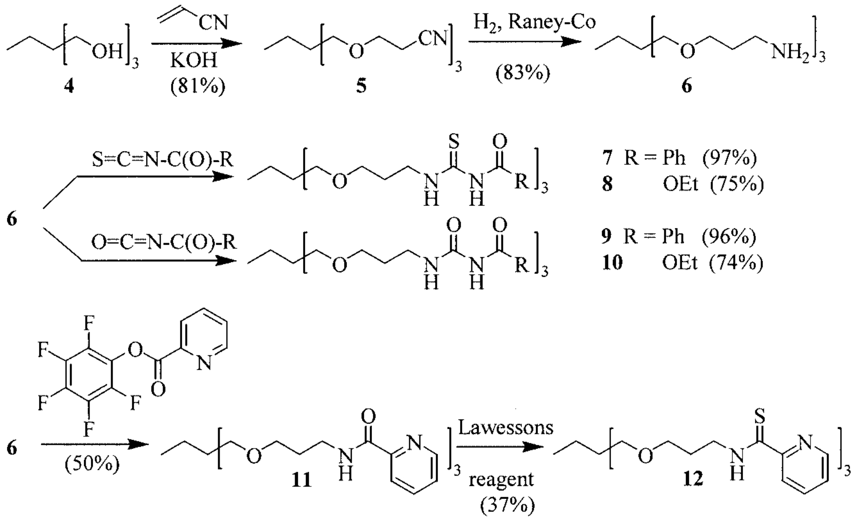
Scheme 4.

Liquid-Liquid Extractions

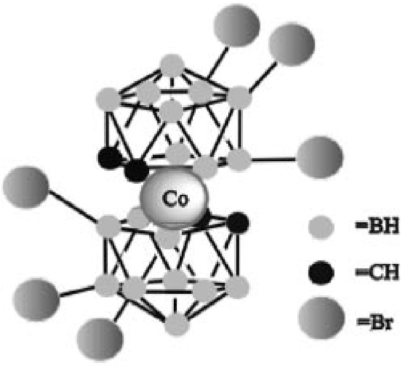
Extractions of Americium and Europium

In order to study whether compounds **7**–**11** are good ionophores for the separation of actinides from lanthanides in nuclear waste treatment, liquid-liquid extractions were performed using Am^{3+} and Eu^{3+} as general representatives of actinides and lanthanides, respectively, and because they are present in nuclear waste. The extractions were carried out with *o*-nitrophenyl hexyl ether (NPHE) as the organic phase at varying nitric acid concentrations with and without hexa-



Scheme 3.

brominated cobalt bis(dicarbollide) anion (Br_6-COSAN) as a synergistic agent (Scheme 5). Br_6-COSAN is a lipophilic anion that facilitates the transport of the cations to the organic phase as was found for calixarenes.[23]



Scheme 5.

The experiments were carried out at different pH values, ranging from a 0.001 M to 4 M concentration of nitric acid, imposed by the need to simulate the strongly acidic conditions required in the reprocessing of nuclear waste, and with and without Br_6-COSAN as a synergistic agent.

All compounds behave more or less in the same way when the extractions were performed in the absence of Br_6-COSAN, being not effective and not selective, with distribution coefficients for Am^{3+} and Eu^{3+} $\leq 10^{-3}$. However, *N*-acylurea derivative **10** exhibits higher distribution coefficients for Am^{3+} than a *N*-acylurea tetrafunctionalized cavitand,[24] especially at high nitric acid concentrations (D = 0.03 vs. 10^{-3} at 2–3 M nitric acid). Disappointing were the results obtained with picolinamide derivative **11**, which shows no affinity and no selectivity for Am^{3+} and Eu^{3+}.

Upon the addition of Br_6-COSAN as a synergist a considerable enhancement of the extraction properties is achieved (Table 1). Halogenated cosan is used as a synergistic agent in several industrial processes for separation of ^{137}Cs, ^{90}Sr, Ln, and Ac (e.g. the UNEX[25] process) and is very effective either itself (Cs extraction), either with polyethylene glycols (Sr extraction) or CMPO (Ln, Ac extraction). In all cases the distribution coefficients increase, the most pronounced at 0.001 M HNO_3. The high distribution coefficients (>1000 at 0.01 M and 0.001 M HNO_3) obtained with picolinamide derivative **11** are remarkable. For the *N*-acyl(thio)urea derivatives **7**–**10** the distribution coefficients range between 0.5 and 770 at $\leq$0.01 M HNO_3; at acidities $\geq$0.1 M the distribution coefficients are low. In the case of the corresponding cavitands distribution coefficients between 0.1 and >100 were obtained under the same extraction conditions.[24]

Picrate Extractions

In order to study the extraction behavior of compounds **7**, **8**, **9**, and **11** towards other cations [Na^+, K^+, Ag^+, Ca^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, Cu^{2+}, Fe^{3+}, and Eu^{3+} (for comparison reasons)], picrate extraction experiments were performed. The results, expressed as a percentage of cation extracted (%*E*) are collected in Table 2 and shown graphically in Figure 1. Significant differences in complexation can be observed depending on the chelating groups [*N*-acyl(thio)ureas and picolinamide]. Picolinamide derivative **11** shows a very low extraction affinity towards most of the cations examined (in general%$E < 20$).

From Table 2 it is clear that thiourea **8** is a better transfer agent than **7** and **9**; it has higher extraction values for all the cations studied. All the *N*-acyl(thio)urea derivatives show a high preference for Ag^+, especially thiourea **8**, the extraction value (84%) of which is comparable to those obtained with *N*-acylthiourea-tetrafunctionalized cavitands and sulphur-containing calix[4]arene-based ionophores.[26] In the case of the cavitands there is a large difference in the extraction profile of acylthioureas vs. acylureas, but, the tripodal systems do not show this difference. There is a larger difference between the two *N*-acylthiourea derivatives (**7** vs. **8**) than between thiourea **7** and urea **9** (Figure 1). Ionophore **8** with –C(O)OEt moieties is a more effective extractant than **7** containing –C(O)Ph groups. This can be explained by the fact that –C(O)OEt moieties interact stronger than –C(O)Ph groups with hard and soft Lewis acids.[27] In addition, the –C(O)OEt substituents are smaller and more flexible than the –C(O)Ph moieties.

Picolinamide derivative **11** is a less efficient extractant than the *N*-acyl(thio)urea derivatives. Although picolinamide moieties are known to form strong complexes with

Table 1. Distribution coefficients for the extraction of Eu^{3+} and Am^{3+} by tripodal derivatives **7**–**11** in the presence of Br_6-COSAN as a synergist.

Ionophore[a]	Cation	HNO_3 concentration					
		0.001 M	0.01 M	0.1 M	1 M	2 M	4 M
7	Eu^{3+}	109.00	0.553	0.020	0.004	0.001	0.006
	Am^{3+}	73.30	1.28	0.030	0.005	0.006	0.017
8	Eu^{3+}	26.30	2.96	0.036	0.013	0.015	0.008
	Am^{3+}	58.90	3.99	0.043	0.021	0.035	0.051
9	Eu^{3+}	109.00	0.492	0.017	0.005	0.002	0.0119
	Am^{3+}	84.20	0.794	0.033	0.009	0.006	0.009
10	Eu^{3+}	770.00	57.50	0.440	0.068	0.041	0.037
	Am^{3+}	586.00	56.00	0.448	0.063	0.016	0.057
11	Eu^{3+}	>1000	>1000	15.50	5.19	2.99	1.71
	Am^{3+}	>1000	>1000	18.80	6.82	5.34	2.71

[a] Aqueous phase: 152-Eu; 241-Am/[HNO_3] variable ($\approx$1500 kBq/L)/(Sp Gamma D3/0.5 mL). Organic phase: 10^{-3} M ligand + 3.10^{-3} M Br_6-COSAN in NPHE.

Table 2. Percentage of the cation extracted (%E) by tripodal derivatives **7**, **8**, **9**, and **11**.

Ionophore[a]	Na^+	K^+	Ag^+	Ca^{2+}	Cd^{2+}	Hg^{2+}	Pb^{2+}	Cu^{2+}	Fe^{3+}	Eu^{3+}
7	13	26	69	22	18	41	21	33	24	22
8	18	32	84	25	25	56	42	43	29	24
9	20	34	70	27	29	45	24	42	25	21
11	13	10	5	9	12	44	12	16	20	12

[a] $[L]_{o,ini} = 10^{-3}$ M; $[M^{n+}]_{w,ini} = 10^{-4}$ M; $[LiPic]_w = 10^{-4}$ M; $[HNO_3]_w = 10^{-3}$ M; pH = 3.

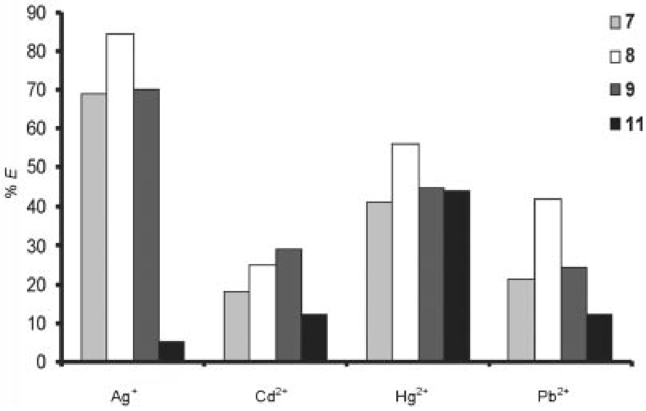


Figure 1. Extraction percentages of silver and heavy-metal ions in CH_2Cl_2 at 25 °C by tripodal derivatives **7**, **8**, **9**, and **11**.

Cu^{2+},[28] the extraction efficiency of **11** for Cu^{2+} is low (16%). On the other hand, **11** has a remarkably high affinity for Hg^{2+} compared to Ag^+ (44% vs. 5%). Probably, the observed selectivity originates from the presence of a hard (C=O group) and a soft (pyridine) donor atom due to the harder character of Hg^{2+} in comparison with Ag^+.

Potentiometric Studies

The selectivities of compounds **7**–**13**, in terms of the potentiometric selectivity coefficients ($K^{pot}_{i,j}$), were evaluated using polymeric membrane-based ion-selective electrodes (ISEs). The polymeric membrane was composed of compounds **7**–**13** as the ionophore (1 wt.-%), poly(vinyl chloride) (PVC; 33 wt.-%) as polymer matrix, *o*-nitrophenyl octyl ether (*o*-NPOE; 66 wt.-%) as the plasticizer, and potassium tetrakis[3,4-bis(trifluoromethyl)phenyl] borate (KTFPB; 30% mol relative to the ionophore) for the purpose of reducing the membrane resistance and suppressing the permeation of counter anions from the aqueous phase into the membrane phase.

To obtain unbiased $K^{pot}_{i,j}$values, the calibration plots for various cations were collected starting from the most discriminating ones.[29] The preliminary selectivity order for each ionophore was established after the preliminary screening of the electrode selectivities. The electrodes exhibited a Nernstian or near-Nernstian response in pure solutions of moderately and highly discriminating cations, at least within the range 10^{-3}–10^{-1} M. When a flattering (or a reversing) of the calibration curves was observed, the selectivity coefficients were obtained from the Nernstian part of the response curve at lower activities.

The logarithmic values of the selectivity coefficients calculated for Pb^{2+} as the primary cation (log $K^{pot}_{i,j}$) are presented in Figure 2 and Figure 3. It is well known that electrodes with membranes containing only KTFPB exhibit a potentiometric selectivity pattern related to the lipophilicity of the cations. The results obtained for membranes containing *N*-acyl(thio)ureas **7**–**10** and picolin(thio)amide derivatives **11**–**13** revealed that ionophores **7**–**13** induce considerable changes in the electrode selectivity compared to ion-exchanger (KTFPB). This confirms that compounds **7**–**13** are able to form complexes with cations and the selectivity of such interactions affects the potentiometric selectivity of ISEs. The behavior of *N*-acyl(thio)ureas **7**–**10** in the membrane is more or less the same, except for UO_2^{2+} cations. For electrodes with membranes containing *N*-acylurea derivative **9** much larger potentiometric selectivities toward the harder UO_2^{2+} were observed than in the cases of *N*-acylthiourea derivatives **7** and **8**. The latter ionophores **7** and **8** have soft ligating C=S groups. Therefore the electrodes with membranes based on these ionophores showed an enhanced selectivity towards Ag^+, compared to membranes with only cation-exchanger.

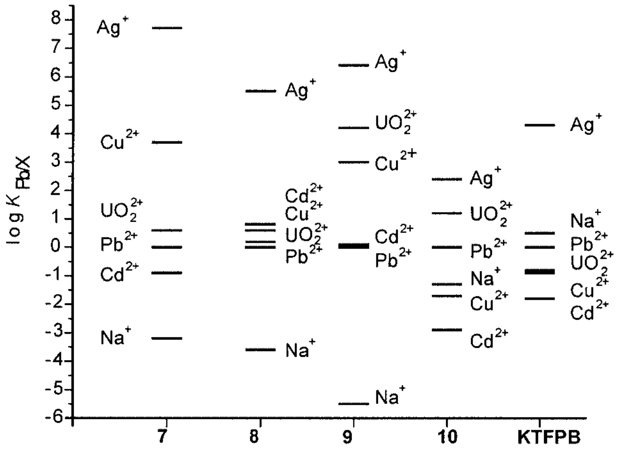


Figure 2. Selectivity coefficients for electrodes prepared with PVC/*o*-NPOE (1:2 by weight) membranes containing *N*-acyl(thio)urea derivatives **7**, **8**, **9**, and **10** and lipophilic sites (KTFPB), as well as membranes without ion-exchanger only, with Pb^{2+} as the primary cation.

Electrodes with picolin(thio)amide derivatives **11**–**13** exhibited a pronounced decrease of the selectivity towards Ag^+ ion. For these ionophores high selectivity coefficients for mercury over lead ions (log $K^{pot}_{Pb,Hg}$) were determined. It should be mentioned, however, that the values of $K^{pot}_{Pb,Hg}$ for **11** and **12** are only roughly estimated, because during the

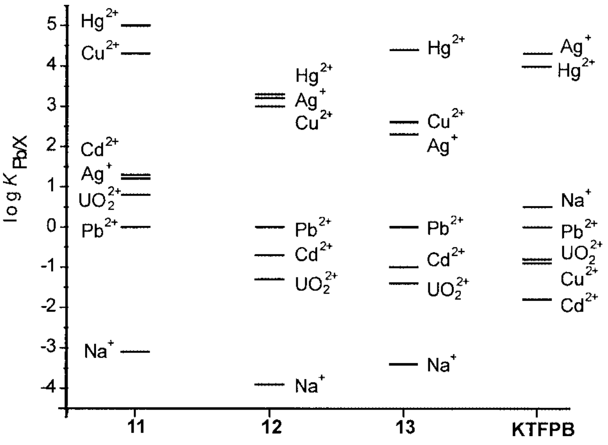


Figure 3. Selectivity coefficients for electrodes prepared with PVC/*o*-NPOE (1:2 by weight) membranes containing picolin(thio)urea derivatives **11**, **12**, and **13** and lipophilic sites (KTFPB) as well as membranes with ion-exchanger only, with Pb^{2+} as the primary cation.

first calibration in mercury nitrate solutions the electrodes responded to Hg^{2+} ions in a super-Nernstian fashion. Moreover, after 24 hours contact of the membrane with a 10^{-2} M mercury nitrate solution, the electrode lost its initial selectivity and the response to Hg^{2+}. An anionic response was observed in solutions with concentrations of $>10^{-3}$ M mercury nitrate. This could indicate a very strong and irreversible complexation of Hg^{2+} by picolinamide **11** (in concordance with the high extraction data found by the picrate method; vide supra). Moreover, all membranes that contain *N*-acylthioureas or picolin(thio)amides provided an increased selectivity towards Cu^{2+} in comparison with the membranes doped with *N*-acylureas and without ionophore. The log $K^{pot}_{Pb,Cu}$ values for picolin(thio)amides **11** and **12** are again roughly estimated. It should be noted, that a subsequent change in the color of the membranes in time was observed upon conditioning in $Cu(NO_3)_2$ or $Hg(NO_3)_2$ solutions, suggesting certain redox processes occurring within the membrane.

It is well established that selectivity coefficients for neutral carrier-based membranes are typically related to the differences in the free energies of solvation of the ions in the sample and membrane phase, the stability constants of the ion-ionophore complexes in the membrane, and the concentrations of the ionophore and the ionic sites in the membrane.[30] However, the main factor that is primarily responsible for changes in the potentiometric selectivity of ionophore-based polymeric membrane ion-selective electrodes reflects the relative stability constants of complexes formed by an ionophore with primary and interfering ions within the membrane phase.

The complex formation constants were determined by means of the segmented sandwich method.[31] The values of the complex formation constants for chosen cations are collected in Table 3. The values of *N*-acylthiourea **8** and picolin(thio)amides **11** and **12** for Cu^{2+} have to be treated as an approximation due to the non-linear response of the membranes with **8**, **11**, and **12** to the logarithm of the Cu^{2+} activity in sample solutions. The same holds for *N*-acylurea **9** towards Ag^+. Unfortunately, this is a limitation of the method.

Among the examined tripodal ionophores, *N*-acylurea **10** forms the weakest complexes with cations. Significantly strong complexes with Cu^{2+} were formed by the ionophores **7**, **9**, and **11**, while *N*-acylthiourea derivatives **7** and **8** exhibit an enhanced interaction with Cd^{2+}.

From a comparison of the data of picolinamide model compound **13** with those of tripodal picolinamide **11**, it is clear that the attachment of three picolinamide moieties to the tripodal platform led to significant differences of their selectivity coefficients (Table 2) and to higher complex formation constants for most of the studied cations. This clearly demonstrates the positive effect on the extraction properties by bringing together chelating groups.

Conclusions

A series of simple C_3-symmetrical trimethylolpropane-based ionophores with *N*-acyl(thio)ureas **7**–**10** and picolin(thio)amides **11** and **12** ligating sites were prepared. *N*-Acylurea derivative **10** exhibits high separation factors for Am^{3+} and Eu^{3+} at very low nitric acid concentrations for Am^{3+}/Eu^{3+} separation, but the distribution coefficients are low. In all cases the extraction efficiency was considerably enhanced upon addition of Br_6-COSAN as a synergist. In the case of the tripodal picolinamide derivative **11** a distribution coefficient of > 1000 was obtained.

N-acyl(thio)ureas **7**–**10** are good ionophores for the extraction and detection of Ag^+, especially compound **8**, which has the highest affinity (84%); the extraction profile

Table 3. Formal complex formation constants, log β_{ML}, obtained with ionophores **7**–**13** in PVC/*o*-NPOE (1:2) membranes, using the segmented sandwich method.

Cation[a]	*N*-acyl(thio)urea				Picolin(thio)amide		
	7	**8**	**9**	**10**	**11**	**12**	**13**
Ag^+	9.6	11.7	>10.3	5.1	5.2	6.1	6.5
Na^+	5.4	7.0	7.7	4.7	5.8	6.6	6.5
Cu^{2+}	19.6	>15.7	21.8	12.1	>20.4	>11.3	10.4
Cd^{2+}	16.0	16.3	12.4	10.3	15.0	14.4	10.0
Pb^{2+}	12.5	14.6	13.7	10.2	14.8	16.3	8.1
UO_2^{2+}	14.9	15.4	15.4	11.0	13.6	12.4	8.3

[a] Standard deviations ≤ 0.3 (from at least three replicate measurements). The stoichiometries of the ion-ionophore were assumed to be 1:1.

is comparable to those obtained with preorganized ligands (cavitands, calixarenes). Picolinamide derivative **11** is a very good ionophore for Hg^{2+} extraction in the presence of other metals, e.g. Ag^+. This is remarkable, since Ag^+ is as Hg^{2+} a soft metal. *N*-acylurea **9** has a very high complexation constant for Cu^{2+} cations, which is in agreement with the result obtained from picrate extractions. Picolin(thio)amide tripodal compounds **11** and **12** form complexes with Cu^{2+} and Hg^{2+} so strong that they cannot be used as ionophores in polymeric membrane-based ion-selective electrodes, although they are very useful ionophores for liquid-liquid extractions.

Experimental Section

General Remarks: ^{1}H and ^{13}C NMR spectra were recorded with a Varian Unity INOVA (300 MHz) and a Varian Unity 400 WB NMR spectrometer, respectively. All spectra were recorded in $CDCl_3$. Residual solvent protons were used as internal standard and chemical shifts are given in ppm relative to tetramethylsilane (TMS). Fast atom bombardment (FAB) mass spectra were measured with a Finnigan MAT 90 spectrometer using *m*-nitrobenzyl alcohol (NBA) as a matrix. All solvents were purified by standard procedures. All other chemicals were analytically pure and were used without further purification. All reactions were carried out under an inert argon atmosphere.

Compound **13** was prepared following a literature procedure.[22]

1,1,1-Tris[(aminopropoxy)methyl]propane (6): A solution of tris(cyanoethyl) tripodand **5** (1.00 g, 3.41 mmol), ammonia (25%, 10 mL) and Raney-Co (catalytic amount) in methanol (35 mL) was placed in an autoclave and a hydrogen atmosphere (7 bars) was applied for 5 h. After the reaction, the mixture was flushed with nitrogen. The Raney-Co was filtered off on a glass filter with hyflo and the solvent evaporated in vacuo to give **6** as a yellow oil. Yield 867 mg (83%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.86 (t, J = 7.7 Hz, 3 H, CH_3), 1.20 (q, J = 7.7 Hz, 2 H, CH_2), 1.63–1.70 (m, 6 H, CH_2), 2.80 (t, J = 6.6 Hz, 6 H, CH_2NH_2), 3.23 (s, 6 H, CH_2O), 3.42 (t, J = 6.2 Hz, 6 H, OCH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 7.0, 23.9, 39.3, 42.7, 69.6, 71.9 ppm. FAB-MS: *m/z* calcd. for $C_{15}H_{35}N_3O_3$ 306.0; found 306.2 $[M + H]^+$.

General Procedure for the Preparation of (Thio)urea Tripodal Compounds 7–10: A solution of 1,1,1-tris[(aminopropoxy)methyl]propane (**6**) and the appropriate iso(thio)cyanate in acetonitrile (50 mL) was heated at reflux overnight. Upon cooling dichloromethane (50 mL) was added and the mixture was washed with water (3 × 100 mL). After drying with $MgSO_4$ the solvent was evaporated to give the pure *N*-acyl(thio)urea tripodal compounds **7**–**10**.

Benzoyl Thiourea Tripodand 7: Compound **7** was prepared from **6** (1.10 g, 3.60 mmol) and benzoyl isothiocyanate (1.46 mL, 10.8 mmol) as a yellow oil. Yield 2.76 g (97%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.86 (t, J = 7.5 Hz, 3 H, CH_3), 1.45 (q, J = 7.5 Hz, 2 H, CH_2), 1.82–1.90 (m, 6 H, CH_2), 3.25 (s, 6 H, CH_2O), 3.42–3.60 (m, 6 H, OCH_2), 3.79 (q, 6 H, J = 6.6 Hz, CH_2NH), 6.80–6.85 (m, 3 H, CH_2*NH*CO), 7.00–7.50 (m, 9 H, Ar*H*), 7.54–7.89 (m, 6 H, Ar*H*), 9.02 (s, 3 H, CS*NH*CO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 7.0, 27.5, 28.5, 38.5, 43.0, 68.0, 71.0, 127.0, 128.5, 131.0, 133.0, 167.0, 179.0 ppm. FAB-MS: *m/z* calcd. for $C_{39}H_{50}N_6O_6S_3$ 794.3; found 794.1 $[M + H]^+$.

Ethoxycarbonyl Thiourea Tripodand 8: Compound **8** was prepared from **6** (1.05 g, 3.44 mmol) and ethoxycarbonyl isothiocyanate (1.2 mL, 10.6 mmol) as a yellow oil. Yield 1.80 g (75%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.81 (t, J = 7.3 Hz, 3 H, CH_3), 1.29 (t, J = 7.1 Hz, 9 H, CH_3), 1.42 (q, J = 7.3 Hz, 2 H, CH_2), 1.87–1.95 (m, 6 H, CH_2), 3.30 (s, 6 H, CCH_2O), 3.42 (t, J = 5.8 Hz, 6 H, OCH_2), 3.78 (q, J = 6.6 Hz, 6 H, CH_2NH), 4.20 (q, J = 7.1 Hz, 6 H, OCH_2), 8.18 (s, 3 H, *NH*), 9.70 (s, 3 H, *NH*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 7.0, 14.0, 22.5, 24.0, 42.0, 43.0, 62.0, 68.5, 71.0, 152.0, 178.5 ppm. FAB-MS: *m/z* calcd. for $C_{27}H_{50}N_6O_9S_3$ 698.3; found 698.2 $[M + H]^+$.

Benzoyl Urea Tripodand 9: Compound **9** was prepared from **6** (1.19 g, 3.90 mmol) and benzoyl thiocyanate (1.5 mL, 11.9 mmol) as a yellow oil. Yield 2.79 g (96%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.81 (t, J = 7.3 Hz, 3 H, CH_3), 1.26 (q, J = 7.3 Hz, 2 H, CH_2), 1.81–1.91 (m, 6 H, CH_2), 3.48 (s, 6 H, CH_2O), 3.41–3.51 (m, 12 H, OCH_2 + CH_2NH), 7.44–7.47 (m, 9 H, Ar*H*), 7.51–7.57 (m, 6 H, Ar*H*), 9.00 (s, 3 H, *NH*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 7.5, 22.5, 28.0, 38.0, 43.5, 68.0, 71.0, 124.0, 124.5, 128.0, 128.5, 166.0, 179.0. FAB-MS: *m/z* calcd. for $C_{39}H_{50}N_6O_9$ 747.6; found 747.4 $[M + H]^+$.

Ethoxycarbonyl Urea Tripodand 10: Compound **10** was prepared from **6** (850 mg, 2.78 mmol) and ethoxycarbonyl isocyanate (0.87 mL, 8.35 mmol) as a yellow oil. Yield 1.33 g (74%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.81 (t, J = 7.1 Hz, 3 H, CH_3), 1.25 (t, J = 7.1 Hz, 9 H, CH_3), 1.38 (q, J = 7.1 Hz, 2 H, CH_2), 1.75–1.81 (m, 6 H, CH_2), 3.25 (s, 6 H, CH_2O), 3.40 (q, J = 6.6 Hz, 6 H, CH_2NH), 3.45 (t, J = 5.8 Hz, 6 H, OCH_2), 4.44 (q, J = 7.1 Hz, 6 H, OCH_2), 7.35 (s, 3 H, *NH*), 7.82 (s, 3 H, *NH*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 7.5. 13.5, 22.5, 29.0, 37.0, 42.5, 62.0, 68.0, 71.0, 128.0, 153.0. FAB-MS: *m/z* calcd. for $C_{27}H_{50}N_6O_{12}$ 650.3; found 650.2 $[M + H]^+$.

Tris(picolinamide) Tripodand 11: A solution of 1,1,1-tris[(aminopropoxy)methyl]propane (**6**) (1.32 g, 4.32 mmol) and pentafluorophenyl picolinate[32] (5.25 g, 19.44 mmol) in dry THF (60 mL) was stirred for 5 days. Subsequently, water (60 mL) was added, whereupon the mixture was extracted with dichloromethane (3 × 50 mL). The organic layer was washed with aqueous sodium hydrogencarbonate (100 mL), brine (100 mL), and dried with $MgSO_4$. Evaporation of the solvent gave a brown oil, which was purified by flash chromatography (SiO_2, EtOAc/hexanes, 2:1) to afford pure **11** as a brownish oil. Yield 1.34 g (50%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, J = 7.7 Hz, 3 H, CH_3), 1.62 (q, J = 7.7 Hz, 2 H, CH_2), 1.88 (q, J = 5.8 Hz, 6 H, CH_2), 3.47 (s, 6 H, CH_2O), 3.52 (t, J = 5.8 Hz, 6 H, OCH_2), 3.60 (q, J = 5.8 Hz, 6 H, CH_2NH), 7.40 (t, J = 4.7 Hz, 3 H, ArH), 7.85 (t, J = 7.7 Hz, 3 H, ArH), 8.20 (d, J = 7.7 Hz, 3 H, Ar*H*), 8.36–8.38 (m, 3 H, *NH*), 8.52 (d, J = 4.7 Hz, 3 H, Ar*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 7.5, 22.0, 28.0, 37.0, 42.5, 69.5, 71.0, 122.0, 125.5, 136.5, 145.0, 162.0 ppm. FAB-MS: *m/z* calcd. for $C_{33}H_{44}N_6O_6$ 621.3; found 621.4 $[M + H]^+$.

Tris(picolinthioamide) Tripodand 12: A mixture of **11** (100 mg, 0.16 mmol) and Lawesson's reagent (212 mg, 0.53 mmol) in toluene (35 mL) was refluxed for 5 h. The solvent was evaporated and the residue purified by column chromatography (SiO_2, EtOAc followed by a gradient of EtOAc/MeOH, 97:3) to give **12** as a brownish oil. Yield 50 mg (37%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.79 (t, J = 7.7 Hz, 3 H, CH_3), 1.62 (q, J = 7.7 Hz, 2 H, CH_2), 1.79 (q, J = 5.8 Hz, 6 H, CH_2), 3.38 (s, 6 H, CH_2O), 3.43 (t, J = 5.8 Hz, 6 H, OCH_2), 3.49 (q, J = 5.8 Hz, 6 H, CH_2NH), 7.40 (t, J = 4.7 Hz, 3 H, ArH), 7.85 (t, J = 7.7 Hz, 3 H, ArH), 8.28–8.30 (m, 3 H, *NH*), 8.20 (d, 3 H, J = 7.7 Hz, Ar*H*), 8.42 (d, J = 4.7 Hz, 3 H, Ar*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 7.7. 22.8, 28.0, 37.9, 43.2, 70.2, 71.6, 122.1, 125.9, 137.1, 147.9, 150.1, 164.2 ppm. FAB-MS: *m/z* calcd. for $C_{33}H_{44}N_6O_3S_3$ 669.5; found 669.0 $[M + H]^+$.

Liquid-Liquid Extractions of Americium and Europium: The aqueous phase was chosen to simulate real occurring waste solutions. An aqueous phase was prepared at varying concentrations of nitric acid (0.01–4 M). Europium, as radioisotope ^{152}Eu, and americium, as radioisotope ^{241}Am, were added at an activity around 1500 kBq dm^{-3}, which corresponds approximately to a concentration of 5×10^{-8} M for Am and 1.5×10^{-9} M for Eu.

A 10^{-3} M solution of the extractant (in most of the cases) in *o*-nitrophenyl hexyl ether (NPHE) was used as the organic phase. Equal volumes (1 mL) of both phases were shaken in sealed tubes for half an hour. Then 0.5 mL of each phase was collected and the concentration of actinide and lanthanide in each phase was determined by gamma counting (Eurysis Ge coaxial-EGPC 15 type P). The distribution coefficients of the cations are defined by D where $\Sigma[M_\mathrm{org}]$ and $\Sigma[M_\mathrm{aq}]$ denote the total concentration of the metal species in the organic and in the aqueous phase, respectively:

$$D = \frac{\Sigma[M_\mathrm{org}]}{\Sigma[M_\mathrm{aq}]}$$

Picrate Extractions. Solutions: The 10^{-4} M salt stock solutions were prepared by dissolving the required amounts of the appropriate metal nitrate $M^{n+}(NO_3^-)_n$ and LiPic in 10^{-3} M HNO_3 adjusting the total volume of the solution to 100 mL using volumetric glassware. The pH of the solutions was close to pH 3, and adjusted to pH 3 by adding small amounts of LiOH. The metal picrate solutions were prepared in situ in the stock solutions. The 10^{-3} M stock solutions of the ligands were prepared by dissolving the appropriate amount of ligands in 20 mL of CH_2Cl_2.

Procedure: Equal volumes (1.0 mL) of the organic and the aqueous solutions were transferred into a stoppered glass vial and stirred at ambient temperatures (about 23 °C) for 17 h. The solutions were disengaged by centrifugation (1600 rpm for 10 min). The concentration of picrate ion in the aqueous and organic phase was determined spectrophotometrically (λ_max = 355 nm). Each measurement was repeated three times. Blank experiments showed that no picrate extraction occurred in the absence of ionophore. The percentage of the cation extracted into the organic phase ($\%E = E\times100\%$), 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_w), is expressed by the following equation:

$$\%E = [A_\mathrm{o}/(A_\mathrm{o} + A_\mathrm{w})]\times100\%$$

Potentiometric Measurements. Reagents: The salts and membrane components potassium tetrakis[3,4-bis(trifluoromethyl)phenyl]borate (KTFPB), *o*-nitrophenyl octyl ether (*o*-NPOE), high molecular weight poly(vinyl chloride) (PVC), and tetrahydrofuran (THF, distilled prior to use) and all salts were purchased from Fluka (Ronkonkoma, NY). Aqueous solutions were obtained by dissolving the appropriate salts in Nanopure purified distilled water.

Membrane Preparation: The polymeric membranes evaluated for the potentiometric ion response and used for the determination of stability constants contained ionophore (20 mmol/kg), KTFPB (2 mmol/kg) in PVC/*o*-NPOE (1:2 by weight) polymeric matrix (unless otherwise indicated in the text). The membrane components (total 140 mg) were dissolved in freshly distilled THF (1.4 mL). The solution was placed in a glass ring (22 mm i.d.) mounted over a glass plate and then covered with another glass plate to slow down the solvent evaporation. After 24 hours, the resulting membrane was peeled from the glass plate and discs of 7 mm diameter were cut out. The procedure for the preparation of the polymeric membranes evaluated for the potentiometric ion response was similar to the one described above. The total amount of membrane components was 200 mg and the membranes consisted of 1 wt.-% of ionophore, 30 mol% of KTFPB and PVC/*o*-NPOE (1:2 by weight).

Potentiometric Response to Cations and Selectivity Measurements: Membrane discs were mounted in conventional ISE electrode bodies (Type IS 561; Philips, Eindhoven, The Netherlands) for electromotive force (EMF) measurements. All measurements were performed at ambient temperature (22 ± 1 °C) using a galvanic cell of the following type: Ag/$AgCl_{(s)}$/3 M KCl/bridge electrolyte/sample/ion-selective membrane/inner filling solution/$AgCl_{(s)}$/Ag. The bridge electrolyte consisted of 1 M lithium acetate. The inner filling solution of the ISEs was a 0.01 M solution of NaCl. The EMF values were measured using a custom made 16-channel electrode monitor. Details of this equipment have been described previously.[33]

The performance of the electrodes was examined by measuring the EMF for solutions of examined cations over the concentration range of 10^{-7}–10^{-1} M.

Potentiometric selectivity coefficients were determined by the separate solution method (SSM) according to the modification of the method described in literature.[30] Selectivity coefficient $K_{i,j}^\mathrm{pot}$ values were obtained from adequate, unbiased E^0 measurements for each ion, according to the equation:

$$K_{i,j}^\mathrm{pot} = \exp\{\frac{z_\mathrm{i}F}{RT}\cdot(E_j^0 - E_j^0)\}$$

where R, T, and F are the gas constant, absolute temperature, and the Faraday constant, respectively. The charge of primary ion, i, is indicated as z_i and measured potentials for primary and interfering ions are put as E_i^0 and E_j^0, respectively.

Activity coefficients were calculated according to the Debye–Hückel approximation.[34]

Determination of the Stability Constants: Experiments were carried out according to the procedure described in literature.[31] Two sets of membranes were prepared: Membranes with and without ionophore. A series of 7 mm i.d. membrane discs were cut from the parent membrane, and these disks were conditioned over 2–3 days in appropriate salt solutions [$1\cdot10^{-1}$ M NaCl, 10^{-2} M $CuCl_2$, $1\cdot10^{-2}$ M $CdCl_2$, $5\cdot10^{-3}$ M $PbCl_2$, $1\cdot10^{-3}$ M $AgNO_3$, $1\cdot10^{-3}$ M $UO_2(NO_3)_2$/$1\cdot10^{-3}$ M NaCl (pH = 4)]. After drying of the individual membranes, the sandwich membrane was made by attaching of the membrane with ionophore to the membrane without ionophore. The segmented membrane was then mounted into a Philips electrode body (membrane with ionophore faced the sample solution) and immediately immersed into an appropriate salt solution (identical as for conditioning of the membrane). The potential was recorded as the mean of the last minute of a 10 min measurement period in the appropriate salt solution. The potential of the electrodes with sandwich membranes remained free of diffusion-induced drifts for 20–50 min, depending on the ionophore incorporated within the membrane and the ion measured. Membrane potential values ΔEMF were calculated by subtracting the cell potential for a membrane without ionophore from that of the sandwich membrane. The formation constant, $\beta_{i\mathrm{L}_n}$, was calculated from the following equation:

$$\beta_{i\mathrm{L}_n} = (L_T - \frac{n}{z_\mathrm{i}}R_T^-)^{-n}\cdot\exp(\frac{z_\mathrm{i}F}{RT}\Delta EMF)$$

where: n is the complex stoichiometry, L_T and R_T are the concentrations of ionophore and ionic site additives in the membrane, respectively.

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