CHELATING AGENTS FOR ACTINIDE/LANTHANIDE SEPARATION

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Cover details: The triangle in the glass tube contains the world’s first sample of americium, produced in 1944. Reproduced with permission of Ernest Orlando Lawrence Berkeley National Laboratory.

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PROEFSCHRIFT

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A mis padres y hermana

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Chapter 1
General Introduction

In nuclear power plants the energy released by fission of uranium atoms is used to produce electricity. After the mining, the raw uranium ore goes through a variety of chemical processes to extract, mill, concentrate, and refine the uranium in a suitable form for use in a nuclear reactor. Most of the nuclear reactors in the world are of the light water type. For these reactors it is necessary to enrich the natural uranium (*e.g.* by ultra centrifugation of gaseous UF_6) in uranium-235 between 3-5% (mined uranium ore contains only 0.7% of the uranium-235 isotope with the reminder uranium-238). Once the uranium is purified and converted into uranium oxide (UO_2), it is incorporated into fuel assemblies for the reactor.[1]

These fuel assemblies are inserted into the reactor where the nuclear fission reactions that generate energy take place. The nuclear fission reactions generate highly radioactive waste, which is deposited in deep geological repositories. This spent fuel will remain toxic and radioactive for hundreds of thousands of years, essentially due to the presence of plutonium and the minor actinides neptunium, americium, and curium. All the processes in which fuel is involved together form the so-called nuclear fuel cycle.

The fuel cycle shown in Figure 1.1 has a step called reprocessing before the waste disposal. The main reasons for reprocessing are the recovery and recycling of fissionable isotopes. Uranium-235 and the highly radiotoxic plutonium-239 are recovered from the process stream and recycled or prepared for long-term geological storage.[2,3] However, the remaining waste still contains minor actinides. By partitioning (chemical separation) and transmutation (radionuclide conversion), the amount of long-lived components of nuclear waste can be reduced.[4,5,6]

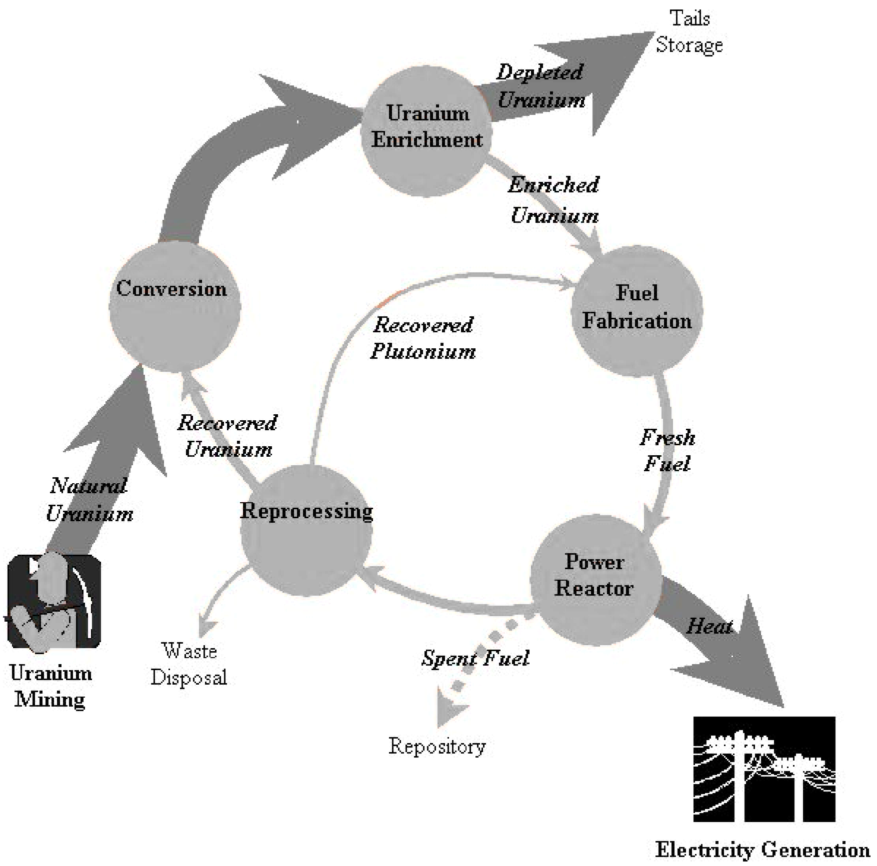

Figure 1.1. Representation of a nuclear fuel cycle.[7]

Nowadays, partitioning and transmutation are topics of intensive research. In the transmutation process minor actinides with long-term radioactivity are converted into isotopes with short-term radioactivity upon bombardment with neutrons.[8] The separation of actinides from lanthanides is very important. Lanthanides and actinides are chemically 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 in the nuclear waste mixture.

Lanthanides are 10 to 20 times more abundant than the actinides americium and curium after reprocessing of the nuclear waste. In order to effectively transmutate actinides, it is of vital importance to improve the methodology for the separation of lanthanides and actinides. This Thesis deals with the synthesis and evaluation of potential ionophores for the separation of trivalent actinides (americium), in the presence of trivalent lanthanides (europium), from the highly acidic waste generated during reprocessing.

In Chapter 2 the different commonly employed partitioning processes are described. Special attention is paid to the hydrochemical process and to different lanthanide/actinide coextractants and selective extractants that can be used in this process. In addition, an overview is given of the known ligands that specifically bind actinides/lanthanides.

Based on the results obtained previously in our group[9] for actinide/lanthanide separation, in Chapter 3 different, novel cavitand-based ionophores are described. Liquid-liquid extractions of lanthanides and actinides from aqueous nitric acid into dichloromethane or *o*-nitrophenyl hexyl ether (NPHE) are performed both in the absence and presence of the hexabrominated cobalt bis(dicarbollide) anion (Br_6-COSAN) as a synergistic anion.

In Chapter 4 the binding properties of the ionophores synthesized in Chapter 3 towards different cations such as Pb^{2+}, Cu^{2+}, Ag^{+}, Hg^{2+}, Cd^{2+}, Eu^{3+}, Fe^{3+}, K^{+}, Na^{+}, and Ca^{2+} are studied, as well as the incorporation in ion selective electrodes (ISEs).

In Chapter 5 the superior properties of COSAN-containing cavitands as americium/europium extractants, compared with the corresponding ionophores without COSAN, are reported.

Chapter 6 deals with the synthesis of different ionophores based on trimethylolpropane. The results of liquid-liquid extractions towards different cations, including americium and europium, and their behavior in ISEs are described.

In Chapter 7 the synthesis and liquid-liquid extraction behavior of two CMP(O) tripodands and their derivatives are reported. In addition to ISEs studies towards different cations, the extractions with two CMP(O) tripodand derivatives attached to magnetic silica particles for magnetically assisted chemical separation of europium and americium are reported.

References

[1] *The Nuclear Fuel Cycle*, Uranium Information Center (UIC), Melburne, **2001**.

[2] Gruppelaar, H.; Kloosterman, J. L.; Konings, R. J. M. *Advanced Technologies for the Reduction of Nuclear Waste*, Petten: Netherlands Energy Research Foundation, ECN-R-98-008, **1998**.

[3] Lang-Lenton Leon, J. *NEA News*, 19.1, **2001**.

[4] *Actinide and Fission Product Partitioning and Transmutation*, Nuclear Energy Agency (NEA), Paris, OECD, 2000 (Sixth International Information Exchange Meeting, Madrid, Spain).

[5] *Waste Management in the Nuclear Fuel Cycle*, Uranium Information Center, Melbourne, **2004**.

[6] Jacquet, L. *Partitioning and Transmutation as a Waste Management Option in a Future Nuclear Era*, Rapport de la Commission Ampere, MINECOBEL, **2001**.

[7] *Brief Outline of the Nuclear Fuel Cycle*, Annual Report 1998-99, Australian Safeguards and Non-Proliferation Office (ASNO), **1999**.

[8] MacIlwain, C. *Nature* **2000**, *405*, 498.

[9] Boerrigter, H. *Cavitand Selective Carriers for Trivalent Actinides,* Ph. D. Thesis, University of Twente, **1998**.

Chapter 2

Nuclear Waste Treatment: Partitioning Process

Nuclear fission energy generation gives rise to highly radioactive waste. If inadequately managed, the nuclear waste could constitute a potential risk for future generations. This Chapter deals with the different partitioning processes that are under investigation for the successful treatment of nuclear waste. The hydrochemical process will be discussed in more detail, with special attention to lanthanide/actinide coextractants and selective extractants that are/can be used in this process.

2.1 Introduction

Nuclear power plants use uranium as fuel to generate energy.[1,2,3] The nuclear waste generated, in all the processes involving the fuel for electric power generation in a nuclear reactor, is one of the most harmful environmental problems due to all the products that it contains. In addition to the still slightly enriched uranium, the spent fuel from power production reactors contains moderate amounts of transuranium (TRU) actinides (plutonium and the so-called minor actinides) and fission products, which are very long-living radionuclides.

For the last fifty years of nuclear power plant operation, prior to deposition of the waste in deep geological repositories reprocessing has taken place. The driving force behind the industrial reprocessing of nuclear waste fuel is to exploit the fissionable material to a maximum, *i.e.* to optimize the sustainability of nuclear power by recycling. In this classical fuel cycle, uranium and plutonium are recovered in the aqueous Plutonium Uranium Refining by Extraction (PUREX)[4,5] process and they can be used for new reactor-fuel fabrication. However, the remaining liquid (raffinate) contains the minor actinides (americium, neptunium, and curium) and fission products of which some are long-lived (such as isotopes of technetium, cesium, and iodine). Together, these form the high-level waste (HLW) to be disposed off.

The main concern in the disposal of radioactive waste is related to long-lived radionuclides – some of them will remain hazardous for tens of thousands of years. By partitioning (chemical separation) and transmutation (radionuclide conversion), it is possible to reduce the long-lived components of the high level liquid waste. The partitioning can be achieved by an advanced aqueous process (hydrochemical) or by a dry process (pyrochemical).

This Chapter is mainly focused on the description of the extractants used for coextraction of minor actinides (Am^{3+}, Cm^{3+}) and lanthanides, and for selective extraction of trivalent actinides from the high level liquid waste generated during the PUREX process.

2.2 PUREX process

Three different options can be distinguished in the PUREX process according to which the partitioning of transuranium elements (TRUs) (Np, Pu, Am, and Cm) can be achieved. The standard PUREX process and the improved PUREX process are well known, whereas the extended PUREX process is still in the phase of research and development.

The standard and the improved PUREX process are basically the same. In both processes tetravalent uranium and plutonium are separated from the high-level waste by dissolution of the fuel in nitric acid and solvent extraction by tri-*n*-butylphosphate (TBP) in a kerosene-type aliphatic hydrocarbon diluent as the extractant. The minor actinides (Np, Am, Cm) and fission products remain, which are conditioned in a glass matrix for storage and final disposal. The trivalent americium and curium are not extracted by TBP. They remain in the raffinate high level liquid waste (HLLW) of the first cycle, together with the bulk of fission products, except gaseous products like ^{85}Kr and ^{129}I, which are separated in the off-gas of the spent fuel dissolution. In the standard process neptunium is partially extracted by TBP from the spent fuel, whereas the total removal of neptunium is achieved by oxidation of Np^{5+} (in the spent fuel) to Np^{6+} (extractable using TBP) in the improved process. The extended PUREX process[6,7] includes the separation of minor actinides (Am and Cm) and some fission products, mainly lanthanides, from the HLLW. For this separation there are three alternatives. One is based on the coextraction of minor Ac^{3+} and Ln^{3+} (fission products). The other two are based on the selective extraction of minor actinides from HLLW either by oxidation of the Ac^{3+} and Ac^{4+} to a higher oxidation state followed by an extraction process or using selective extractants to separate Ac^{3+} from Ln^{3+}. For the coextraction of minor actinides and lanthanides different processes are under development, *viz.* TRUEX, DIAMEX, DIPDA, TALSPEAK, and TRPO.

2.2.1 TRUEX

The TransUranium Extraction (TRUEX) process was developed by Argonne National Lab, USA, during the eighties,[8] for the recovery of all the actinides from various types of highly acidic nuclear waste solutions. It is based on octyl(phenyl)-*N*,*N*-

diisobutylcarbamoylmethylphosphine oxide (CMPO) **1** (R^1 = octyl, phenyl; R^2 = isobutyl) as the principal extractant (Chart 2.1). The TRUEX extractant is usually a mixture of 0.2M CMPO and 1.2M tri-*n*-butylphosphate (TBP) in *n*-dodecane.[9,10] TBP prevents the formation of a third phase, contributes to better acid dependencies for the extraction of americium, and reduces hydrolytic and radiolytic degradation of CMPO.

2.2.2 DIAMEX

The DIAMide EXtraction (DIAMEX) process was developed by CEA in France, which uses *N,N'*-dimethyl-*N,N'*-dibutyl-2-tetradecylmalonamide (DMDBTDMA) **2** (R^1 = methyl; R^2 = butyl; R^3 = tetradecyl) as extractant (Chart 2.1).[11,12] This malonamide dissolves in *n*-dodecane and does not give a third phase when it is in contact with 3-4M HNO_3. The advantages of this process are the use of an incinerable extractant (leading to reduced secondary waste) and the ease of extractant synthesis. More recently, a new diamide [*N,N'*-dimethyl-*N,N'*-dioctyl-2-hexylethoxymalonamide (DMDOHEMA) **2** (R^1 = methyl; R^2 = butyl; R^3 = hexyl)] was selected by the CEA for the design of an improved DIAMEX process.[13]

2.2.3 DIDPA and TALSPEAK

The DIPDA process was developed at the JAERI, Japan, and employs diisodecylphosphoric acid **3** as extractant,[14,15] whereas bis(2-ethylhexyl)phosphoric acid (HDEHP) **4** with TPB in *n*-dodecane is used in the TALSPEAK process, which was developed at the CTH in Sweden (Chart 2.1).[16] Both processes have in common the use of phosphoric acid derivatives as extractants. The removal of Am^{3+} and Cm^{3+} from the loaded organic phase is achieved using DTPA (diethylenetriaminopentaacetic acid) or lactic acid as complexing agents.[17]

In the DIPDA process trivalent actinides can only be extracted at very low HNO_3 concentrations (~0.5M).[18]

The addition of *N*-piperidinomethane-1,1-diphosphonic acid (PMDPA) to the aqueous phase of the TALSPEAK process makes HDEHP (**4**) a better extractant for lanthanides.[19]

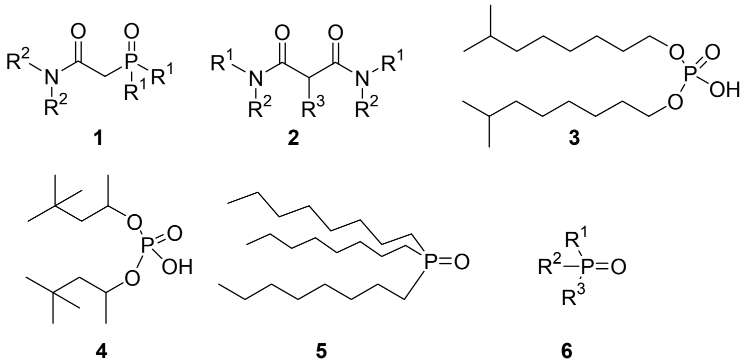

Chart 2.1. Structures of different coextractants used in coextraction processes: **1**: CMPO, **2**: malonamide, **3**: DIPDA, **4**: HDEHP, **5**: TOPO (component of TRPO), **6**: trialkylphosphine oxide.

However, both processes have two major problems, *viz.* third phase formation and formation of secondary waste. Third phase formation appears at low pH and is unfavorable for the design of an effective separation process, because the concentration of metals is limited in comparison with the amount of extractant required. The secondary waste can be reduced using hydrazine carbonate (a salt free reagent that can easily be decomposed) as back-extractant of tri- and tetravalent lanthanides/actinides from bis(2-ethylhexyl)phosphoric acid (HDEHP) **4**[20] and diisodecylphosphoric acid (DIPDA) **3**.[21]

2.2.4 TRPO

The TRPO process, developed in China, uses a mixture of trialkylphosphine oxides (TRPOs) **6**, which are very good extractants for actinides, lanthanides, and other fission products from HNO_3 and HLW solutions (Chart 2.1).[22] The extractant mixture has the advantage of being a liquid, which is completely inmiscible with all commonly used hydrocarbons, and being inexpensive. In this process the actinides are stripped with 5M HNO_3 to recover Am, Cm, and rare earth metals, with 0.5M oxalic acid to recover Np and Pu, and with 5% Na_2CO_3 to recover U.[23,24]

Table 2.1. Summary of coextraction process for separation of minor actinides from nitric acid solutions.

Country	Process name	Advantages	Disadvantages
USA	TRUEX	Very efficient Large pH range	
France	DIAMEX	Incinerable extractant Efficient	
Japan	DIPDA		More secondary waste Limited extraction pH adjustment
China	TRPO	Cheap extractant High radiation stability	Degradation products

2.3 Pyrochemical processing

The long-lived component of the high-level waste can also be reduced by a pyrochemical process.[25,26,27,28] In general, pyrochemical processes are individual or combined processes which take place at high temperatures in the absence of water. Such processes (volatilization, liquid-liquid extraction with molten salt, electrorefining in non-aqueous media, vacuum distillation, fractional crystallization, melt refining, zone melting, and gas solid reactions) are widely used.

The main objectives of this process for nuclear waste treatment are: i) the selective extraction of uranium, plutonium and minor actinides (Np, Am, and Cm), ii) minimization of losses of the relevant elements in the various process steps, and iii) generation of smaller waste volumes in comparison with the PUREX process.

The pyrochemical processes have found their most important use in the recycling of plutonium for nuclear weapons manufacture, because they remove ^{241}Am produced by the radioactive decay of ^{241}Pu.

The advantages of these processes are that the high-level waste can be treated within a short period of time (a few months) in comparison with the PUREX process, which needs at least five years and that gives smaller waste volumes. However, it has some disadvantages like the difficulty to separate individual transuranium elements, the need of high operation temperatures and a highly pure atmosphere, which requires the use of sophisticated technology, and the difficulty to develop a process for continuous operation.

2.4 Lanthanide complexation*

With the lanthanides, or rare-earth metals, the first electrons appear in the f-orbitals in the ground state configurations of the elements. The chemical properties of the lanthanides are highly uniform; all lanthanide ions have a 3+ oxidation state in common. However, cerium (Ce) and europium (Eu) can have a stable 4+ and 2+ oxidation state, respectively, in water.[29]

The most common coordination numbers are 8 and 9. The considerable change in size of the lanthanide ions going from La^{3+} (1.17 Å) to Lu^{3+} (1.00 Å) makes that the coordination number varies from 10-11 for La^{3+} to 8-9 for Lu^{3+}.[30] Lanthanide ions have hard acidic properties, as indicated by the preference for fluoride anions, oxygen-, and nitrogen-containing ligands.

The design of selective chelating agents is important since these ions are intensively employed in many different applications, *e.g.* as contrast agents for magnetic resonance imaging (MRI),[31] catalysts in RNA hydrolysis,[32] responsive luminescent lanthanide complexes,[33] active agents in radiotherapy,[34] and shift reagents in NMR.[35] For each application, the optimum choice for the chelator is complicated and is based on various physicochemical and chemical criteria[36] such as the binding sites, stereocompatibility, and the stability constant, as well as on biological criteria such as toxicity, biodistribution, and solubility.[37]

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[*] For more detailed information see a recent compilation of reviews on lanthanide chemistry (Special issue "Frontiers in Lanthanide Chemistry", *Chem. Rev.* **2002**, *102*, 1807) or the book edited by Sigel highlighting the role of lanthanide coordination chemistry (Metal Ions in Biological Systems: The Lanthanides and their Interactions with Biosystems, vol. 40, Marcel Dekker (eds.), Basel, **2003**).

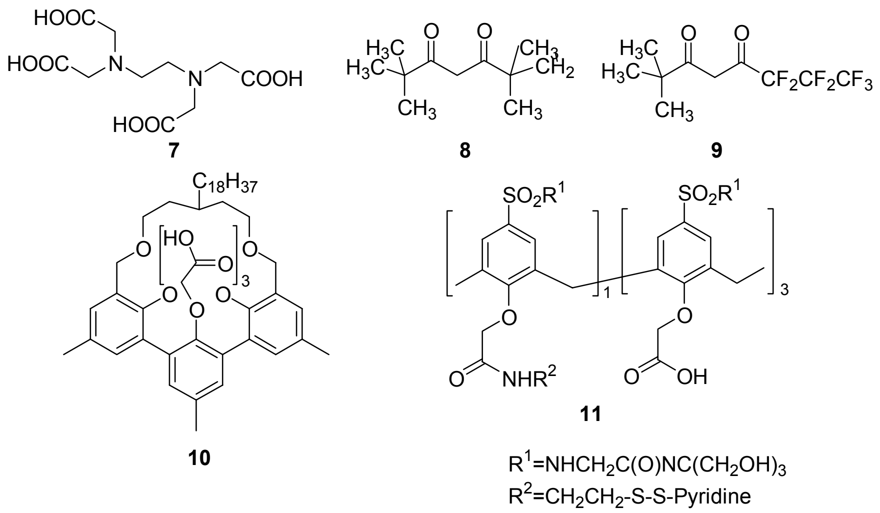
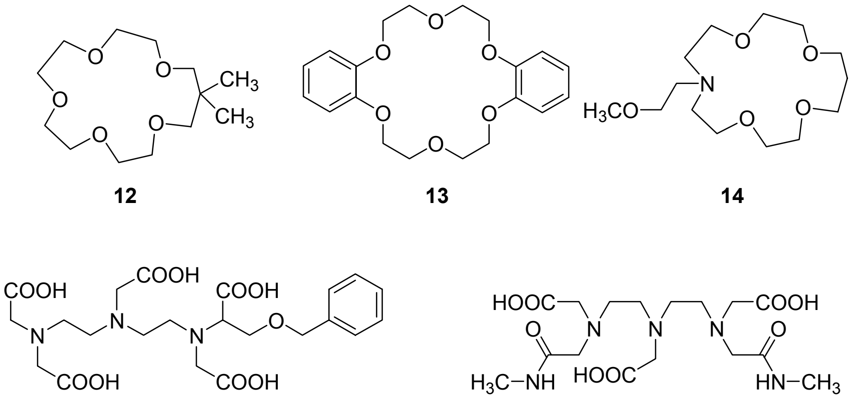


Chart 2.2. Oxygen-containing ligands: **7**: EDTA, **8**, **9**: β-diketonates, **10**: terphenyl based ligand, **11**: calix[4]arene based ligands.

The large number of chelating ligands reported for lanthanide complexation, can be divided into oxygen- and nitrogen-containing ligands.

2.4.1 Oxygen-containing ligands

The most stable and common lanthanide complexes are those with chelating oxygen ligands (Charts 2.2 and 2.3). The use of EDTA-type compounds (**7**) and hydroxo acids such as tartaric or citric acid, for the formation of water-soluble complexes, is of great importance in ion-exchange separations.[38] β-Diketonates (**8**,**9**) have been extensively studied as lanthanide chelating ligands, particularly since some of the fluorinated derivatives (*e.g.* **9**) give complexes that are volatile and suitable for gas-chromatography separations.



12 **13** **14**

15 **16**

Chart 2.3. Oxygen-containing ligands: **12-14**: crown ether derivatives, **15**, **16**: polydentate derivatives.

Other complexes used are based on the *m*-terphenyl moiety (**10**)[39] and calix[4]arenes (**11**),[40,41] which can be easily functionalized with lanthanide complexing groups, *e.g.* carboxylic acids, carboxylates, amides, and phosphonic acids.

In aqueous solution many other types of polyoxo ligands effectively complex Ln^{3+} ions, including polyphosphates, mixed phosphoryl-carbonyl species, and crown ethers (**12-14**). There are many complexes in which polydentate ligands (**15**, **16**) with both oxygen and nitrogen donor atoms are used, leading to high coordination numbers.[42,43]

2.4.2 Nitrogen-containing ligands

Complexes of amines such as terpyridine[44] (**17**, **18**), bipyridine,[45] en[46] (**19**), and dien are known, and coordination numbers of 8, 9, and 10 as in $[Ln(en)_4]^{3+}$, $[Ln(terpy)_3]^{3+}$, and $[Ln(dien)_4(NO_3)]^{2+}$ are typical. Cyclen derivatives have extensively been used. These ligands form strong and stable complexes in water and can be functionalized with four pendant arms containing additional donor groups.[47] Complexes with porphyrins (**22**),[48] porphyrinogens,[49] and phthalocyanines[50] are very well known due to their photochemical and magnetic properties.

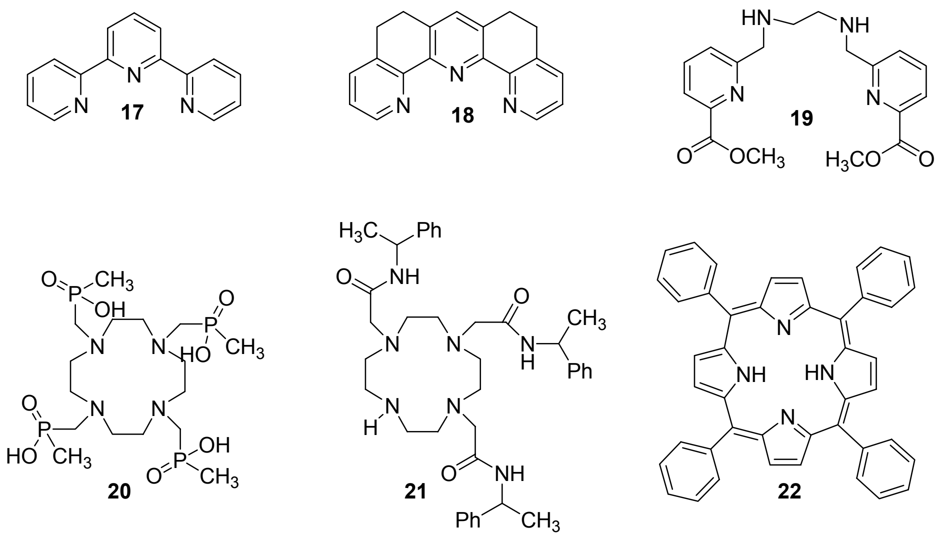
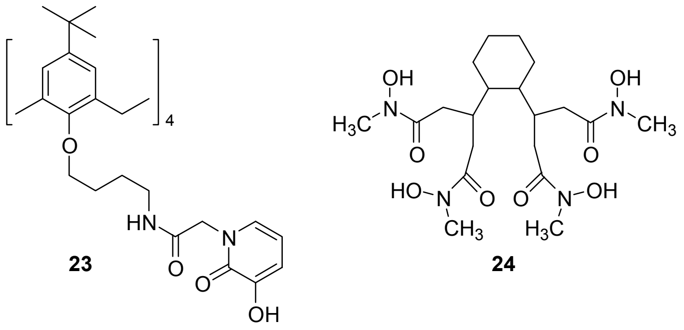


Chart 2.4. Nitrogen-containing ligands: **17**, **18**: terpyridine derivatives, **19**: en derivative, **20**, **21**: cyclen derivatives, **22**: porphyrin.

2.5 Actinide complexation

The fundamental knowledge of the actinides, their basic chemistry, and coordination systems is still relatively early in its development. They are analogous to the lanthanides and result from the filling of the 5f orbitals. Only three actinides are naturally occurring, *viz.* thorium (Th), protactinium (Pa), and uranium (U); the remaining elements are produced artificially. All isotopes of the actinide elements are radioactive.[51]

The common oxidation state of the actinides is trivalent. However, oxidation states higher than 3+ are preferred for the early elements of the block, Th, Pa, U, and Np.[38] In complexes, the Ac^{3+} and Ac^{4+} ions generally display variable and high coordination numbers: 8, 9, 10, or higher. However, due to their large ionic radii the preferred coordination number is 8 in Ac^{3+} and Ac^{4+} complexes, with bidentate chelating agents forming five- or six-membered chelating rings.[52]



23

24

Chart 2.5. 23: hydroxypyridonate derivative, **24**: hydroxamate derivative.

These hard ions preferentially interact with hard acid donor atoms, such as oxygen in carboxylate, alkoxide, or with fluoride anions. Some covalency has been observed in interactions with softer donors, such as chloride, nitrogen, and sulfur.[53]

For actinide complexation many different chelating units have been used. In this Chapter the attention will be mainly focused on the chelating agents able to complex the most common actinides and those most likely to be present in nuclear wastes, namely Pu, Th, Am, U, and Np. Hydroxypyridonate[54,55] (**23**) and hydroxamate[56,57] (**24**) have been used as specific actinide complexating agents (Chart 2.5) for the removal of Pu^{4+}. Ligand **24** is also a drug for in vivo clinical applications. It does not include any aromatic groups and the *N*-substitution of the hydroxamate groups makes it less susceptible to hydrolysis, as compared to previous compounds.[56-58]

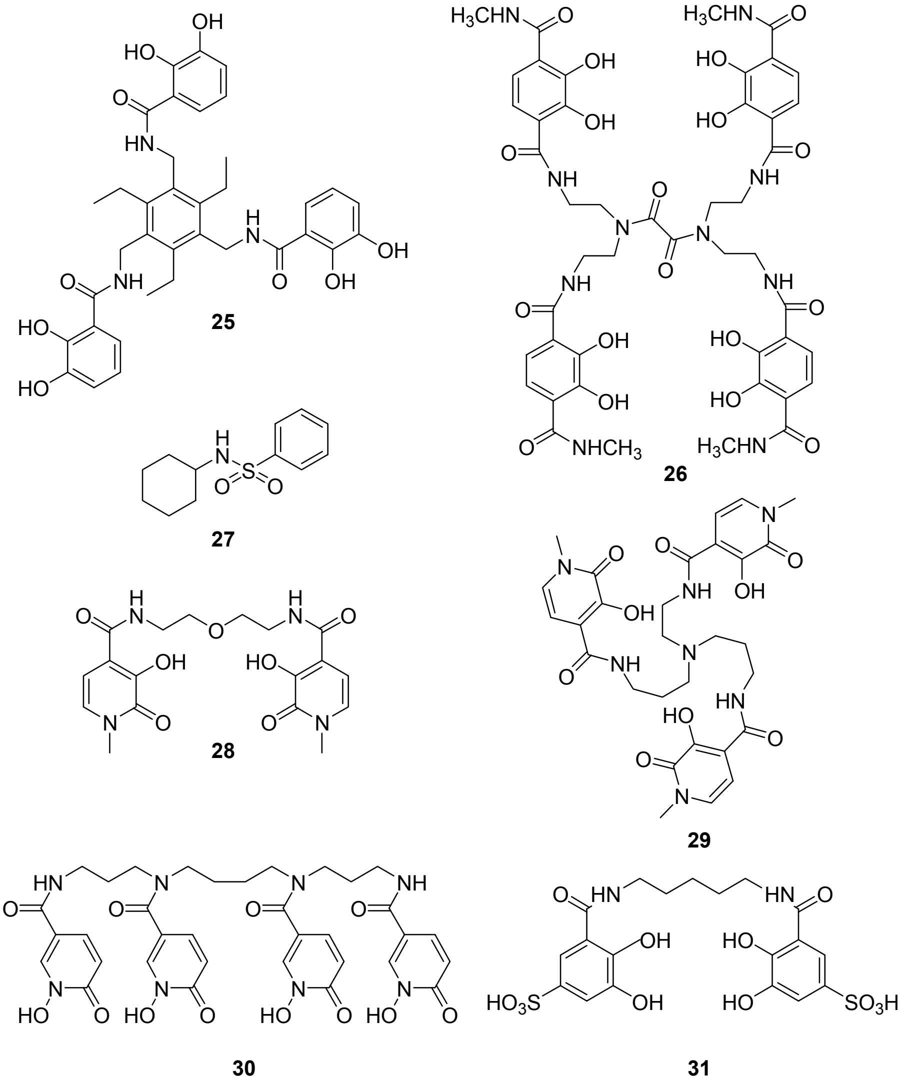
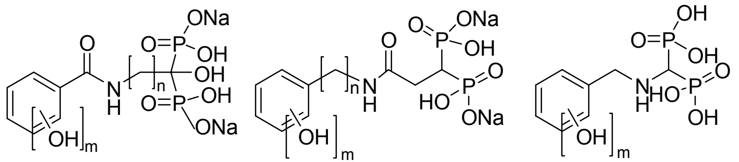


Chart 2.6. Actinide complexing ligands: **25**: EtMECAM, **26**: Oxo-H(2,2)-MeTAM, **27**: Cyhexyl(SFAM), **28**: 5LIO(Me-3,2-HOPO), **29**: TREN(Me-3,2-HOPO), **30**: 3,4,3-LI(1,2-HOPO), **31**: 5-LI-CAM(S).

Catecholate ligands incorporating a variety of electron-withdrawing substituents have been extensively studied for their extraordinary high affinity for metal ions with high oxidation state such as U^{4+} and Th^{4+}.[59] Catecholamide- (CAM) (**25**, **31**), terephthalimide- (TAM) (**26**), sulfonamide- (**27**), and hydroxypyridinone-ligands (HOPO) (**28**-**30**) have been extensively studied by the group of Raymond.[60] Making use of these chelating moieties and a diversity of platforms, different ligands have been synthesized and used as sequestering agents for actinides (Chart 2.6). Three HOPO-based ligands, *viz.* tetradentate 5-LIO-(Me-3,2-HOPO) (**28**), hexadentate TREN(Me-3,2-HOPO) (**29**), and octadentate 3,4,3-LI(1,2-HOPO) (**30**), are considered to be the most competent and robust actinide chelating agents so far.[60] While all three are able to effectively chelate Pu^{4+}, Th^{4+}, U^{6+}, Am^{3+}, Np^{5+}, and Np^{4+}, each ligand is especially suitable for chelation of a specific actinide: **28** for Np^{4+}, **29** for Am^{3+}, **30** for Pu^{4+} and Th^{4+}, and **28** combined with 5-LI-CAM(S) (**31**) for U^{6+}.

Recently, the synthesis of a new type of chelating agents (**32**-**34**) (Chart 2.7) for actinide ion complexation has been reported. These ligands have mixed functional groups such as catechol and bisphosphonic acid in order to enhance the binding affinity for actininide ions. Data concerning the chelating properties of these compounds have not been reported yet.[61]



32 m=2 (2,3), n=3

33 m=2 (3,4), n=2

34 m=2 (2,3)

Chart 2.7. Catechol-bisphosphonate derivatives

2.6 Actinide / Lanthanide coextractants

For the evaluation of an extractant, two properties are important: the distribution coefficient (D) and the separation factor ($S_{M/N}$). The distribution coefficient (equation 2.1) is the ratio between the metal concentration in the organic phase and in the aqueous phase. It should be higher than 1 for an efficient extraction.

$$D = \frac{\sum [M_{org}]}{\sum [M_{aq}]} \tag{2.1}$$

The separation factor ($S_{M/N}$) is expressed as the ratio of the distribution coefficients of the elements that are separated in the extraction (equation 2.2).

$$S_{M/N} = \frac{D_M}{D_N} \tag{2.2}$$

For the coextraction of actinides and lanthanides from the high level liquid waste, different types of compounds are being used, *e.g.* phosphorus containing compounds and amides. These ionophores can be monochelating, dichelating, or trichelating ligands depending on their nature. All of them contain oxygen which is involved in the cation complexation.

2.6.1 Organophosphorus extractants

In the early sixties, Siddall[62] synthesized different bidentate carbamoylphosphonate compounds (CMP) **35** (Chart 2.8). The bifunctional nature of the CMP reduces the competition between HNO_3 and the trivalent actinides/lanthanides for the primary extractant binding site (P=O). In the presence of HNO_3 the amide function is protonated which protects the P=O-metal from an attack by acid.[63]

Above 2M HNO_3 third phase formation takes place in the extraction process, even in the presence of tri-*n*-butylphosphate (TBP). To prevent third phase formation, the addition of a phase modifier (about 2M $NaNO_3$) is necessary.[64] Although CMP derivatives are good extractants, they cannot be used in the TRUEX process because of the need of a salting out agent to maintain the extraction efficiency and to prevent the third phase formation. In order to overcome the problems encountered with the CMP extractants, CMPO derivatives have been developed.

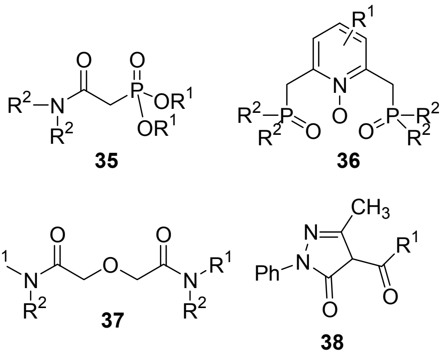


Chart 2.8. Different actinide/lanthanide coextractants: **35**: CMP, **36**: phosphinopyridine *N*-oxide, **37**: diglycolamide, **38**: pyrazolone.

CMPOs **1** (Chart 2.1) are structurally related to CMP moieties **35** (Chart 2.8), but they have a more basic phosphine oxide instead of a phosphonate group. The actinide extraction properties of CMPO derivatives and the phase compatibility vary significantly with the nature of the alkyl substituents on the carbamoylmethylphosphine oxide core. The octyl(phenyl)-*N*,*N*-diisobutyl (CMPO) **1** (R^1=octyl, phenyl; R^2=isobutyl) derivative is the one which has the best combination of properties for actinide extraction in a PUREX-compatible diluent system.[65,66] The isobutyl groups at the amide avoid the formation of a third phase and the octyl and phenyl groups at the phosphorus give the best distribution coefficients (D_{Am}=22.5 from 3M HNO_3 to *n*-dodecane).[8] Due to their good extraction properties, CMPO extractants have received the largest attention of all 'potential' actinide partitioning reagents developed over the past 20 years. As a result they represent the best understood hydrometallurgical extractant for total actinide partitioning from wastes.[9,67,68] However, many studies are still ongoing. A recent example is a study on the effect of the solvent, type, and concentration of a salting-out agent on the extraction abilities of a CMPO-type extractant, diphenyl-*N*,*N*-dimethylcarbamoylmethylphosphine oxide (DPhDMCMPO) **1** (R^1 = phenyl; R^2 = methyl), towards Th^{4+} and Eu^{3+}.[69] By decreasing the polarity of the solvent ($ClCH_2CH_2Cl$ < CH_2Cl_2 < $CHCl_3$) or the concentration of a salting-out agent and by the use of perchlorates as salting-out agents the extraction was enhanced. Unfortunately, no comparison with octyl(phenyl)-*N*,*N*-diisobutylcarbamoylmethylphosphine oxide (CMPO) **1** (R^1 = octyl, phenyl; R^2 = isobutyl) has been reported.

By a combination of two organophosphorus extractants, 0.3M HDEPH **4** and 0.2M CMPO **1** (R^1 = octyl, phenyl; R^2 = isobutyl) in *n*-paraffin as solvent, it is possible to separate lanthanides from actinides in high-level waste solutions (pH=3, $S_{Eu/Am}$=5).[70] This extractant mixture may find useful applications in the partitioning of actinides.

Recently, Paine and coworkers introduced phosphinopyridine *N*-oxides **36** (Chart 2.8), a new type of bifunctional ligands that contain both phosphine oxide and pyridine *N*-oxide donor groups,[71,72] for actinide/lanthanide extraction. Ligands with two phosphine oxide functions strongly chelate with Ln^{3+}, Ac^{3+}, and Ac^{4+} cations with a slight preference for Am^{3+} over Eu^{3+}.[73] In order to achieve a better Am^{3+}/Eu^{3+} separation, softer derivatives have been synthesized with pyridine instead of pyridine *N*-oxide and phosphine sulfide in place of phosphine oxide.[74] Extraction data have not been reported so far.

2.6.2 Amides and diamides

The advantages of *N*,*N*-dialkyl aliphatic amides over organophosphorus compounds have already been identified since the work of Siddall.[75] They are related to the harmless nature of their degradation products and to the possibility to incinerate the used solvent (C, H, O, N-principle, which is based on the use of extractants which only contain these atoms)[76] leading to a minimization of the volume of secondary waste.[77,78]

Malonamides and diglycolamides have received most attention in the last years, due to their good extraction properties and the possibility to incinerate them.

Malonamides are weak bases in which the carbonyl amide groups may bind to a metal ion in a chelate complex.[79] The chemical properties of malonamides **2** (Chart 2.1) are influenced by the nature of the substituents on the nitrogen and the central methylene carbon atom. The mechanism of extraction of metals by malonamides depends on the acidity of the medium, coordination at low acidity and an ion-pair formation at higher acid concentrations.[80] The extraction ability of different malonamides has been evaluated for

Am^{3+} from a nitric acid medium.[81] *N,N'*-dimethyl-*N,N'*-dibutyl-2-tetradecylmalonamide (DMDBTDMA) **2** (R^1 = methyl; R^2 = butyl; R^3 = tetradecyl) is the most promising malonamide at 3-4M HNO_3 and therefore it is used as extractant in the DIAMEX process. The introduction of phenyl substituents on the nitrogen in malonamides or the replacement of the central carbon atom by oxygen decreases the basicity and thus increases the metal extraction.[82] The better extraction properties of *N,N'*-dimethyl-*N,N'*-dioctyl-2-hexylethoxymalonamide (DMDOHEMA) **2** (R^1 = methyl; R^2 = octyl; R^3 = hexylethoxy) has replaced DMDBTDMA **2** (R^1 = methyl; R^2 = butyl; R^3 = tetradecyl) as extractant in an improved DIAMEX process.[83] The pre-organization of two carboxamide groups, so that they are properly oriented for binding (bicyclic diamide ligand), increases till ~ 10^7 times the extraction of Eu^{3+} in comparison with conventional malonamide extractants (DMDBTDMA and DMDOHEMA).[84]

The use of diglycolamides for Ac^{3+} and Ln^{3+} extraction has been discovered at JAERI (Japan). Diglycolamides **37** are tridentate extractants which have a higher extractability than the malonamides for actinides, as was reported by Sasaki and Tachimori (D_{Am}=0.05, [**37**]=10^{-5}M *vs* [malonamides]=10^{-2}M).[85] A number of diamides with different bridges between the amido groups have been studied for Am^{3+} and Eu^{3+} extraction and separation. All of them, including dithioamides, have very low separation factors ($S_{Am/Eu}$=0.1 for **37**). However, it has been proven that substitution of the ether atom for sulfur enhances the extraction of actinides in comparison with the malonamides (D_{Am}=1.2, [diglycolthioamides]=10^{-3}M *vs* [malonamides]=0.03M). The ether oxygen in diglycolamides plays an important role in the chelation of actinides. The length of the alkyl chain attached to the N atom of the amide group controls the distribution ratios and the solubility of the diglycolamide in *n*-dodecane.[86,87]

The primary factor that affects the extraction properties of diamides $(R^1R^2NC(O))_2R^3$ is the linker between the two terminal amide groups. The extraction ability of the diamides for Eu^{3+} and Am^{3+} decreases in the series of R^3=-(-CH_2OCH_2-)->R^3=-(-CH_2OCH_2-)$_2$>>R^3=-(-CH_2-)$_n$.[88] However, selectivities have not been reported.

2.6.3 Pyralozones

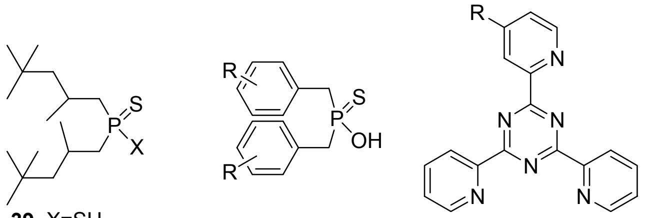
In recent years 4-acylpyrazolones **38** have received considerable attention as chelating agents.[89,90] Because of their increased acidity (relative to β-diketones) and various synthetic modifications, which are possible on the basic structure, these extractants have some possibilities for improved separation procedures for Ac^{3+}/Ln^{3+}.[91] 1-Phenyl-3-methyl-4-benzoyl-5-pyrazolone **38** (R^1 = Ph) has been extensively studied alone[92] or in combination with other reagents, *e.g.* primary ammonium salts, for the extraction of actinides and lanthanides.[93,94,95,96] Umetani et al.[97] reported that the distance between the oxygens, also known as the "bite size", is one of the most significant factors that governs the selectivity for lanthanides in the complexation of β-diketones with metal ions. Recently, it has been shown that better selectivities among the lanthanide series (Nd^{3+}, Eu^{3+}, and Tm^{3+}) can be achieved with 4-acylpyrazolones **38** (R^1 = CH_3, $C(CH_3)_3$, Ph, or CF_3). The presence of a bulky group at the 4-position of the pyrazolone ring makes the "bite size" shorter. The addition of a crown ether as a synergist to 4-acylpyrazolones enhances the extractability of the lanthanides and even improves the selectivities among lanthanides ($S_{Eu/Nd}=47$ with synergist *vs* $S_{Eu/Nd}=19$ without synergist) due to a variety of geometric, enthalpic, and steric effects.[98]

2.7 Selective extractants

After the Plutonium Uranium Refining by Extraction (PUREX) process, trivalent transplutonium elements (TPEs), mainly Am and Cm, and a wide variety of fission products (FPs), involving lanthanides, remain in the high level liquid waste (HLLW). The separation of actinides from the chemically similar lanthanide fission products is a key problem in nuclear reprocessing. For the separation of actinides from the lighter lanthanides, the distribution ratio (D) of the actinides is desirable to be larger than that of the lanthanides. Due to their close similarities, identical charge and similar ionic radii, complexants/extractants containing soft donor atoms (N, S, Cl) are needed to accomplish separation based on the differences between the 4f and 5f metal ion electron shell.[99] Nitrogen, sulfur, and chloro have a lower electronegativity than the oxygen atom, forming a stronger coordinative bond with actinides relative to lanthanides. At this moment the most promising extractants are trimethylpentyl dithiophosphonic acid (Cyanex 301) **39**[100,101] and tripyridyltriazine (TPTZ) **42**.[102]

2.7.1 Cyanex type

The Cyanex compounds belong to the family of organodithiophosphinates, ($R_2PS_2^-$). The replacement of the oxygen in phosphoric acid by sulfur gives them a softer character and enables the extraction to be carried out at very low pH.[103] They have the largest selectivity for Ac^{3+} over Ln^{3+} compared to the other selective extractants. Bis(2,4,4-trimethylpentyl)dithiophosphonic acid (Cyanex 301) **39** is among the most selective ligands ($S_{Am/Eu}$>5000).[104]



39 X=SH
40 OH

41

42

Chart 2.9. Different selective extractants: **39**: Cyanex 301, **40**: Cyanex 302, **41**: aryl dithiophosphonic acid, **42**: 2,4,6-tris(2-pyridyl)-1,3,5-triazine (TPTZ).

Modolo and Odoj[105] synthesized several aryl dithiophosphinic acids (**41**). Separation factors higher than 20 for Am^{3+} over Eu^{3+} were obtained using a mixture of bis(chlorophenyl)dithiophosphonic acid **41** (R = Cl) and tri-*n*-butylphosphate (TBP) or trioctylphosphine oxide. Compared to Cyanex 301 **39**, the aromatic dithiophosphonic acids **41** show a better radiolytic stability and allow a lower pH (pH<3).

Cyanex derivatives can be monodentate or bidentate ligands depending on the structure. In a monothiophosphinate ligand like Cyanex 302 (**40**), both the oxygen and sulfur atoms can bind the cations, making it both bidentate and monodentate. A dithiophosphinate ligand, such as Cyanex 301 (**39**), forms neutral bidentate complexes (ML_3) with no discernible nitrate or water molecules in the inner coordination sphere.[106]

2.7.2 Tridentate nitrogen molecules

Oligoamines[107,108] such as 2,4,6-tris(2-pyridyl)-1,3,5-triazine[109] (**42**) selectively extract actinides in preference to lanthanides from nitric acid solutions into an organic phase. In the presence of 2-bromodecanoic acid as a synergist, separation factors ($S_{Am/Eu}$) of ~10 have been obtained. Another type of tridentate planar ligand is 2,6-bis(5-alkyl-1,2,4-triazol-3-yl)pyridine (**43**), which has even separation factors ($S_{Am/Eu}$) up to 150 in the presence of 2-bromodecanoic acid.[110]

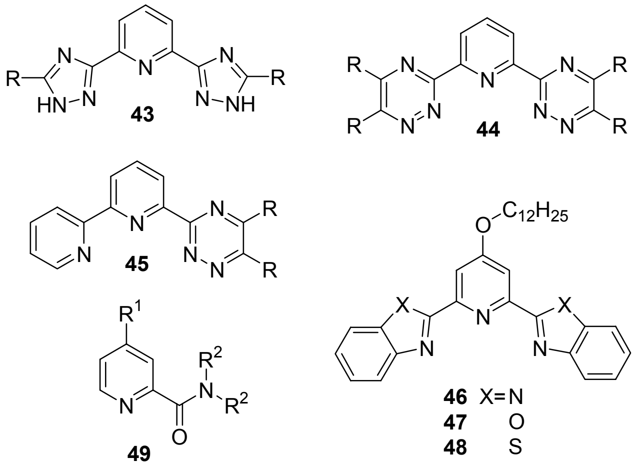


Chart 2.10. Different selective extractants: **43**: 2,6-bis(5-alkyl-1,2,4-triazol-3-yl)pyridine, **44**, BTP, **45**: R,*hemi*-BTPs, **46**: 2,6-bis(benzimidazol-2-yl)pyridine, **47**: 2,6-bis(benzoxazol-2-yl)pyridine, **48**: 2,6-bis(benzothiazol-2-yl)pyridine, **49**: picolinamide.

Comparison studies between bis(triazinyl)pyridine **44** (BTP) and terpyridines **17** showed that BTPs often have larger selectivities than terpyridines ($S_{Am/Eu}$=12 *vs* 7 for BTP and terpyridine, respectively).[111,112] These larger selectivities have been related to the fact that BTPs are able to form single hydrophobic species $[Ln(BTP)_3]^{3+}$ in which three BTP ligands completely fill the primary coordination sphere of the metal.[113] It has been shown that the BTP moiety in a $[Ln(^{i}Pr_4BTP)_3]I_3$ complex binds more tightly to f-block metals than terpyridine in an analogous complex.[114,115]Although BTP reagents have large separation factors, they are sensitive for chemical degradation and radiolysis.[116] Recently, a new class of *N*-heterocycles has been developed, 6-(5,6-dialkyl-1,2,4-triazin-3-yl)-2,2'-bipyridines **43**, also known as R,*hemi*-BTPs, which extraction properties towards lanthanides and actinides are in between those of terpyridines (**17**) and the bis(triazinyl)pyridines (**44**).[117]

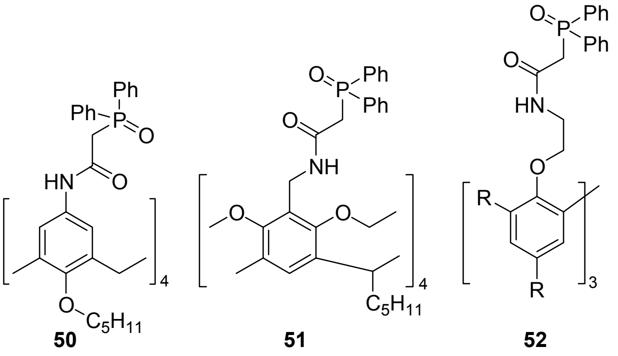
Other interesting, recent ligands based on BTP are 2,6-bis(benzimidazol-2-yl)pyridine **46**, 2,6-bis(benzoxazol-2-yl)pyridine **47**, and 2,6-bis(benzothiazol-2-yl)pyridine **48**. The performance of these terdentate ligands in separations is promising. In the case of 2,6-bis(benzoxazolyl)-4-dodecyloxypyridine **47** separation factors ($S_{Am/Eu}$) up to 70 have been obtained for extractions from 0.02–0.10M HNO_3 in the presence of 2-bromodecanoic acid.[118] Ligand **47** is resistant to hydrolysis and thermal decomposition. Andersson et al.[119] have studied the extraction properties of a mixture of 2,6-bis(benzoxazolyl)-4-dodecyloxypyridine **47** and 2-bromodecanoic acid in *tert*-butylbenzene as a function of ionic strength by varying the nitrate ion and perchlorate ion concentrations. They found that the distribution ratios of Am^{3+} and Eu^{3+} decrease with increasing amounts of H^+, ClO_4^-, and NO_3^-. Increasing the H^+ concentration decreases the extraction efficiency, because the ligand gets protonated. In the case of increasing ClO_4^- concentration, the decrease of the distribution coefficients may be caused by changes in the activities of metal and hydrogen ions in the aqueous phase or in the coordination of the anions around the metal ions in the aqueous phase, giving a higher affinity of the metal ions for the aqueous phase. In the case of nitrate there is an additional effect, *viz.* the formation of Am^{3+} or Eu^{3+} complexes with nitrate in the aqueous phase.

2.7.3 Picolinamides

The first studies with picolinamides (**49**) for actinide/lanthanide separation were developed in France by the CEA.[120] More recently, Korean researchers reported the extraction of Eu^{3+}, Nd^{3+}, and Am^{3+}.[121] They found separation factors up to 9 for Am^{3+}/Eu^{3+} at a concentration of 0.125M HNO_3. This class of compounds combines a moderately hard amide oxygen with a softer pyridine nitrogen binding site.

2.7.4 Platforms

The use of a molecular platform to position ligating sites for actinide/lanthanide complexation was first reported by Böhmer *c.s.* [122,123] Their approach was based on the fact that three CMPOs are involved in the extraction of actinides/lanthanides.[9] They found that attachment of four CMPOs at the lower rim or at the upper rim of a calix[4]arene **50** in the cone conformation resulted in a considerable enhancement of the extraction efficiency toward actinides and lanthanides even at a 10 times lower concentration compared to single CMPO.[124,125] It is remarkable that upper rim CMPO-functionalized calix[4]arenes exhibit selectivity in the trivalent lanthanides series ($D_{La}/D_{Yb} \approx 1000$) and can discriminate between trivalent lanthanides and actinides ($D_{Am}/D_{Eu} \approx 10$) in strongly acidic medium.[126] If the upper rim CMPO-functionalized calix[4]arene is rigidified by a bis(crown ether) at the lower rim, it becomes a more effective extractant than its 'non-locked' counterpart and requires ten times less concentration to obtain the same distribution coefficients.[127] In a recent study of calix[4]arenes with CMPO moieties at the upper rim, they showed that the replacement of secondary amides by tertiary amides resulted in less efficient extractants ($D_{Eu}=0.14$ *vs* 45 of tertiary amide *vs* secondary amide) with less selectivity among the trivalent lanthanides series.[128]



50 **51** **52**

Chart 2.11.

Resorcinarene-based cavitands[129] **51** reported by our group and rigid C_3-symmetric triphenoxymethane[130] **52** have also been used as platforms for actinide/lanthanide separation. In both cases CMPO moieties were anchored to the platform, giving rise to higher efficiencies for Eu^{3+} and higher selectivities within the lanthanide series than the simple CMPO. Unfortunately, no comparison studies with Am^{3+} and Eu^{3+} have been performed.

In addition to CMPO moieties, other chelating groups have also been attached to a platform, *viz.* carboxylic acids, amides, polyaminocarboxylates, and 2,6-bis(benzimidazol-2-yl)pyridines.[125,131,132] Calix[6]arenes, symmetrically functionalized with different chelating groups, *e.g.* carboxylic acid and amide groups, led to high separation factors ($S_{Am/Nd}$=118, at pH=3).[133]

2.8 Outlook

The aim of this Chapter was to give a detailed overview of the partitioning processes, with special emphasis on the coextractants and selective extractants for actinides/lanthanides that can be used in the hydrochemical process.

Although there are a few interesting extractants, there is still a need to develop novel, selective extractants, meeting the specific requirements of the hydrochemical process such as separation of trivalent actinides from the trivalent lanthanides. This Thesis tries to contribute in this direction by the synthesis and evaluation of new extractants able to selectively complex actinides over lanthanides.

Based on the work performed previously in our group, cavitands were initially selected as a platform with CMP(O) and *N*-acyl(thio)urea functions as chelating groups (Chapters 3, 4, and 5). *N*-acylthioureas moieties were introduced due to the soft donor character that they have, which makes them potential candidates for actinide/lanthanide separation.

The last two chapters deal with the synthesis and complexation behavior of a tripodal platform substituted with CMP(O), *N*-acyl(thio)urea, or picolin(thio)amide ligating sites. This type of extractants are more flexible and easier to synthesize than the cavitand derivatives.

The effect of the addition or covalent linkage of the liphophilic hexabrominated cobalt bis(dicarbollide) anion (Br_6-COSAN), on the extraction properties of the new extractants was also investigated.

2.9 References

[1] Baestle, L. H. Burning of Actinides: A Complementary Waste Management Option? IAEA bulletin **1992**, 34, 32.

[2] Schenkel, R.; Magill, J.; Glatz, J. P.; Mayer, K. Partitioning and Transmutation-Technical Feasibility, Proliferation Resistance, and Safe Guardability **2003**, IAEA-SM-367/15/03.

[3] Baetsle, L. H. Application of Partitioning/Transmutation of Radioactive Materials in Radioactive Waste Management **2001**, LNS0212001.

[4] McKay, H. A. C. *The PUREX Process, Part I, Introduction in Science and Technology of Tributyl Phosphate*, Schulz, W. W.; Navratil, J. D. (eds.), CRC Press: Boca Raton, **1984**, p 1.

[5] Miles, J. H. The PUREX Process, Part II, Separation of Plutonium and Uranium in Science and Technology of Tributyl Phosphate, Schulz, W. W.; Navratil, J. D. (eds.), CRC Press: Boca Raton, **1984**, p 11.

[6] Koch, L.; Babelot, J. F.; Glatz, J. P.; Nicolaou, G. Proc. of the 3rd International Exchange Meeting on Actinide and Fission Product Separation and Transmutation, Cadarache, **1994**, OECD/NEA.

[7] Koch, L.; Glatz, J. P.; Konings, R. J. M.; Magill, J. *ITU Annual Report* **1999**, EUR 19054, p 34.

[8] Kalina, D. G.; Horwitz, E. P. *Solvent Extr. Ion Exch.* **1985**, *3*, 235.

[9] Horwitz, E. P.; Kalina, D. G.; Diamond, H.; Vandergift, G. F.; Schulz, W. W. *Solvent Extr. Ion Exch.* **1985**, *3*, 75.

[10] Schulz, W. W.; Horwitz, E. P. *Sep. Sci. Technol.* **1998**, *23*, 1191.

[11] Cuillerdier, C.; Musikas, C.; Hoel, P.; Nigond, L.; Vitart, X. *Sep. Sci. Technol.* **1991**, *26*, 1229.

[12] Madic, C.; Blanc, P.; Condamines, N.; Baron, P.; Berthon, L.; Nicol, C.; Pozo, C.; Lecompte, M.; Philippe, M.; Masson, M.; Hequet, C.; Hudson, M. J. *Actinide Partitioning from High Level Liquid Waste using DIAMEX Process*, Proc. RECOD'94, London (England), **1994**.

[13] Madic, C.; Hudson, M. J.; Liljenzin, J. O.; Glatz, J. P.; Nannicini, R.; Facchini, A.; Kolarik, Z.; Odoj, R. *Prog. Nucl. Energy* **2002**, *40*, 523.

[14] Kubota, M.; Nakamura, H.; Tachimori, S.; Abe, T.; Amano, H. *Proc. Int. Symp. Management Alpha-Contam. Wastes* (Publ. IAEA-SM-246/24), Wien, **1981**, 551.

[15] Morita, Y.; Glatz, J. P.; Kubota, M.; Koch, L.; Pagliosa, G.; Roemer, K.; Nicholl, A. *Solvent Extr. Ion Exch.* **1996**, *14*, 385.

[16] Liljenzin, J. O.; Persson, G.; Svantesson, I.; Wingefors, S. *Radiochim. Acta* **1984**, *35*, 155.

[17] Persson, G.; Svantesson, I.; Wingefors, S.; Liljenzin, J. O. *Solvent Extr. Ion Exch.* **1984**, *2*, 89.

[18] Morita, Y.; Kubota, M. *Solvent Extr. Ion Exch.* **1988**, *6*, 233.

[19] Jensen, M. P.; Nash, K. L. *Solvent Extraction for the 21st Century*, Cox, M.; Hidalgo, M.; Valiente, M. (eds.), London, UK, **2001**, p 1089.

[20] Watanabe, M.; Morita, Y.; Kubota, M.; Tatsugae, R. *Radiochim. Acta* **1999**, *87*, 115.

[21] Watanabe, M.; Tatsugae, R.; Morita, Y.; Kubota, M. J. *Radioanal. Nucl. Chem.* **2002**, *257*, 53.

[22] Zhu, Y.; Jiao, R. *Nucl. Technol.* **1994**, *108*, 361.

[23] Glatz, J. P.; Song, C.; Koch, L.; Bokelund, H.; He, X. *Hot Test of the TRPO Process for the Removal of TRU Elements from HLLW*, Global '95, Versaille (France), **1995**.

[24] Song, C.; Glatz, J. P.; Koch, L.; Bokelund, H.; He, X. A Mathematical Model for the Extraction of Americium from HLLW by 30% TRPO and its Experimental Verification, ISEC'96, Melbourne (Australia), **1996**.

[25] Bean, C.H., Steindler, M. J. National Program for Pyrochemical and Dry Processing of Spent Reactor Fuel, ACS Symposium Series 1980, (Actinide Sep.), American Chemical Society, **1980**, p 117.

[26] Madic, C. Actinide Separation Chemistry in Nuclear Waste Streams and Materials, NEA/NSC/ DOC (97)19, 1**997**.

[27] Ackerman, J. P. *Ind. Eng. Chem. Res*. **1991**, *30*, 141.

[28] McPheeters, C. C.; Pierce, R. D.; Mulcahey, T. P. *Progress in Nuclear Energy*, **1997**, *31*, 175.

[29] Greenwood, N. N., Earnshaw, A.*Chemistry of the Elements*, 2nd ed. Butterworth- Heinemann (eds.), Oxford, UK., **1997**.

[30] Evans, W. J.; Shreeve, J. L.; Ziller, J. W.; Doedens, R. J. *Inorg. Chem*. **1995**, *34*, 576.

[31] Platas-Iglesias, C.; Mato-Iglesias, M.; Djanashvili, K.; Muller, R. N.; Vander Elst, L.; Peters, J. A.; de Blas, A.; Rodriguez-Blas, T. *Chem. Eur. J.* **2004**, *10*, 3579.

[32] Hurst, P.; Takasaki, B. K.; Chin, J. *J. Am. Chem. Soc.* **1996**, *118*, 9982.

[33] Parker, D. *Coord. Chem. Rev.* **2000**, *205*, 109.

[34] Heeg, M. J.; Jurisson, S. S. *Acc. Chem. Res*. **1999**, *32*, 1053.

[35] Reuben, J. *J. Am. Chem. Soc.* **1980**, *102*, 2232.

[36] Hancock, R. D.; Martell, A. E. *Chem. Rev*. **1989**, *89*, 1875.

[37] Burgada, R.; Bailly, T.; Lecouvey, M.; Larue, V.; Leroux, Y. *Eur. J. Org. Chem*. **2001**, 349.

[38] Shriver, D. F.; Atkins, P. W.; Langford, C. H. *Inorganic Chemistry*, 2nd ed.; Oxford Universtiy Press, **1994**.

[39] Oude Wolbers, M. P.; van Veggel, F. C. J. M.; Snellink-Ruel, B. H. M.; Hofstraat, J. W.; Geurts, F. A. J.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1997**, *119*, 138.

[40] Sabbatini, N.; Guardigli, M.; Manet, I.; Ungaro, R.; Casnati, A.; Ficher, C.; Ziessel, R.; Ulrich, G. *New J. Chem.* **1995**, *19*, 137.

[41] Steemers, F. J.; Meuris, H. G.; Verboom, W.; Reinhoudt, D. N.; van der Tol, E. B.; Verhoeven, J. W. *J. Org. Chem.* **1997**, *62*, 4229.

[42] Uggeri, F.; Aime, S.; Anelli, P. L.; Botta, M.; Brocchetta, M.; De Haen, C.; Ermondi, G.; Grandi, M.; Paoli, P. *Inorg. Chem.* **1995**, *34*, 633.

[43] Jászberényi, Z.; Brücher, E.; Jekó, J.; Hideg, K.; Kálai, T.; Király, R. *Eur. J. Inorg. Chem*. **2003**, 3601.

[44] Mallet, C.; Thummel, R. P.; Hery, C. *Inorg. Chim. Acta* **1993**, *210*, 223.

[45] Constable, E. C. *Adv. Inorg. Chem*. **1989**, *34*, 1.

[46] Platas-Iglesias, C.; Mato-Iglesias, M.; Djanashvili, K.; Muller, R. N.; Vander Elst, L.; Peters, J. A.; de Blas, A.; Rodriguez-Blas, T. *Chem. Eur. J.* **2004**, *10*, 3579.

[47] Parker, D. *Coord. Chem. Rev.* **2000**, *205*, 106.

[48] He, H. S.; Zhao, Z. X.; Wong, W. K.; Li, K. F.; Meng, J. X.; Cheah, K. W. *Dalton Trans*. **2003**, 980.

[49] Wang, J.; Dick, A. K. J.; Gardiner, M. G.; Yates, B. F.; Peacock, E. J.; Skelton, B. W.; White, A. H. *Eur. J. Inorg. Chem*. **2004**, 1992.

[50] Zhu, P. H.; Lu, F. L.; Pan, N.; Arnold, D. P.; Zhang S. Y.; Jiang, J. Z. *Eur. J. Inorg. Chem*. **2004**, 510.

[51] *The Chemistry of the Actinide Elements*, 2nd ed.; Katz, J. J., Seaborg, G. T., Morss, L. R. Eds.; Chapman and Hall: London, U. K., **1986**.

[52] Nash, K. L. *Progress and Oportunities,* in *Metal-Ion Separation and Precocentration*, Bond, A. H.; Dietz, M. L.; Rogers, R. M., (eds.), Oxford University Press, Washington, DC, **1999**.

[53] Kaltsoyannis, N.; Scott, P. *The f Elements*, Oxford University Press: New York, **1999**.

[54] Dasaradhi, L.; Stark, P. C.; Huber, V. J.; Smith, P. H.; Jarvinen, G. D.; Gopalan, A. S. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1187.

[55] Lambert, T. N.; Dasaradhi, L.; Huber, V. J.; Gopalan, A. S. *J. Org. Chem.* **1999**, *64*, 6097.

[56] Koshti, N.; Huber, V.; Smith, P.; Gopalan, A. S. *Tetrahedron* **1994**, *50*, 2657.

[57] Gopalan, A. S.; Huber, V. J.; Zincircioglu, O.; Smith, P. H. *J. Chem. Soc., Chem. Commun.* **1992**, 1266.

[58] Santos, M. A.; Rodrigues, E.; Gaspar, M. *J. Chem. Soc., Dalton Trans.* **2000**, 4398.

[59] a) Sofen, S. R.; Abu-Dari, K.; Freyberg, D. P.; Raymond, K. N. *J. Am. Chem. Soc*. **1978**, *100*, 7882; b) Sofen, S. R.; Cooper, S. R.; Raymond, K. N. *Inorg. Chem*. **1979**, *18*, 1611.

[60] Gorden, A. E. V.; Xu, J.; Raymond, K. N.; Durbin, P. *Chem. Rev.* **2003**, *103*, 4207.

[61] Xu, G.; Yang, C.; Liu, B.; Wu, X., Xie, Y. *Heteroatom Chem.* **2004**, *15*, 251.

[62] Siddall, T. H., Jr. *J. Inorg. Nucl. Chem.* **1963**, *25*, 883.

[63] Horwitz, E. P.; Muscatello, A. C.; Kalina, D. G.; Kaplan, L. *Sep. Sci. Technol.* **1981**, *16*, 417.

[64] Rapko, B. M.; Lumetta, G. J. *Solvent Extr. Ion Exch*. **1994**, *12*, 967.

[65] Horwitz, E. P.; Martin, K. A.; Diamond, H.; Kaplan, L. *Solvent Extr. Ion Exch.* **1986**, *4*, 449.

[66] Rapko, B. M. Synthesis, Characterization and Actinide Extraction Behaviour of Bridged Modified Carbamoylmethyl-phosphonates and Phosphine Oxides, in Separations of f-Elements, Nash, K. L.; Choppin, G. R. (eds.), Plenum, Press, New York, **1995**, p 99.

[67] Takeuchi, M.; Tanaka, S.; Yamawaki, M.; Tachimori, S. *J. Nucl. Sci. Technol.* **1995**, *32*, 450.

[68] Mincher, B. J. *Solvent Extr. Ion Exch.* **1992**, *29*, 615.

[69] Yaftian, M. R.; Hassanzadeh, L.; Eshraghi, M. E.; Matt, D. *Sep. Pur. Technol.* **2003**, *31*, 261.

[70] Dhami, P. S.; Chitnis, R. R.; Gopalakrishnan, V.; Wattal, P. K.; Ramanujam, A.; Bauri, A. K. *Sep. Sci. Technol.* **2001**, *36*, 325.

[71] Gan, X.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **2001**, *41*, 4420.

[72] Rapko, B. M.; Duesler, E. N.; Smith, P. H.; Paine, R. T.; Ryan, R. R. *Inorg. Chem.* **1993**, *32*, 2164.

[73] Nash, K. L.; Lavallette, M.; Borkowski, M.; Paine, R. T.; Gan, X. *Inorg. Chem.* **2002**, *41*, 5849.

[74] Gan, X.; Duesler, E.; Parveen, S.; Paine, R. T. *J. Chem. Soc., Dalton Trans.* **2002**, 2328.

[75] Siddall, T. H., Jr. *J. Phys. Chem.* **1960**, *64*, 1863.

[76] Schmidt, E.; Zamorani, E.; Hage, W.; Gaurdini, S. *Assessment Studies on Nuclear Transmutation of By-product Actinides*. European Communities, Joint Research Center Ispra Establishment, **1983**, IX, 114 S.

[77] Codamines, N.; Musikas, C. *Solvent Extr. Ion Exch.* **1992**, *10*, 69.

[78] Musikas, C. *Sep. Sci. Technol.* **1988**, *23*, 1211.

[79] Siddall, T. H.; McDonald, R. L.; Stewart, W. E. *J. Mol. Spectrosc.* **1968**, *28*, 243.

[80] Chan, G. Y. S.; Drew, M. G. B.; Hudson, M. J.; Iveson, P. B.; Liljenzin, J. O.; Skalberg, M.; Spujth, L.; Madic, C. *J. Chem. Soc., Dalton Trans.* **1997**, 649.

[81] Mahajan, G. R.; Prabhu, D. R.; Manchanda, V. K.; Badheka, L. P. *Waste Manage.* **1998**, *18*, 125.

[82] Spjuth, L.; Liljenzin, J. O.; Hudson, M. J.; Drew, M. G. B.; Ivenson, P. B.; Madic, C. *Solvent Extr. Ion Exch.* **2000**, *18*, 1.

[83] Bisel, I.; Nicol, C.; Charbonnel, M. C.; Blanc, P.; Baron, P.; Belnet, F. Proceedings of the Fifth Information Exchange Meeting on Actinides and Fission Products Partitioning and Transmutation, Mol, Belgium, November, **1998**, 25.

[84] Lumetta, G. J.; Rapko, B. M.; Hay, B. P.; Garza, P. A.; Hutchison, J. E.; Gilbertson, R. D. *Solvent Extr. Ion Exch.* **2003**, *21*, 29.

[85] Sasaki, Y.; Tachimori, S. *Solvent Extr. Ion. Exch.* **2002**, *20*, 21.

[86] Sasaki, Y.; Sugo, Y.; Suzuki, S.; Tachimori, S. *Solvent Extr. Ion Exch.* **2001**, *19*, 91.

[87] Tachimori, S.; Sasaki, Y.; Suzuki, S. *Solvent Extr. Ion Exch.* **2002**, *20*, 687.

[88] Chen, W. J.; Zhu, L.; Ding, S. D.; Liu, Z. Q.; Chen, S. J.; Xia, C.; Huang, Z.; Jing, Y. D. *Solvent Extraction for the 21st Century*, Cox, M.; Hidalgo, M.; Valiente, M. (eds.), London, UK, **2001**, p 259.

[89] Mickler, W.; Reich, A.; Uhlemann, E. *Sep. Sci. Technol.* **1998**, *33*, 428.

[90] Hebrant, M.; Provin, C.; Brunette, J. P.; Tondre, C. *Colloids Surf.* **2001**, *181*, 225.

[91] Reddy, M. L. P. *Solvent Extr. Ion Exch.* **2000**, *181*, 225.

[92] Roy, A.; Nag, K. *J. Inorg. Nucl. Chem.* **1978**, *40*, 331.

[93] Tochiyama, O.; Freiser, H. *Anal. Chim. Acta* **1981**, *131*, 233.

[94] Nash, K. L. *Solvent Extr. Ion Exch.* **1993**, *11*, 729.

[95] Dukov, I. L.; Yordanov, V. M. *Hydrometallurgy* **1998**, *48*, 145.

[96] Dukov, I. L.; Yordanov, V. M.; Atanassova, M. *Solvent Extr. Ion Exch.* **2001**, *19*, 619.

[97] Umetani, S.; Kawase, Y.; Le, Q. T. H.; Matsui, M. *J. Chem. Soc., Dalton Trans.* **2000**, *16*, 2787.

[98] Pavithran, R.; Varma, R. L.; Reddy, M. L. P. *Solvent Extr. Ion Exch.* **2003**, *21*, 797.

[99] Nash, K. L. *Separation Chemistry for Lanthanides and Trivalent Actinides.* Chapter 121, in Handbook on the Physics and Chemistry of Rare Earths, Gschneidner, K. A., Jr.; Eyring, L.; Choppin, G. R.; Lander, G. H. (eds.), **1994**, 197.

[100] Zhu, Y. J.; Chen, J.; Jiao, R. *Solvent Extr. Ion Exch.* **1996**, *14*, 61.

[101] Modolo, G.; Odoj, R. *Solvent Extr. Ion Exch.* **1999**, *17*, 33.

[102] Musikas, C. Actinide/Lanthanide Group Separation using Sulfur and Nitrogen Donor Extractants, in Actinide/Lanthanide Separations, Proc. Int. Symp. Choppin, G. R.; Navratil, J. D.; Schultz, W.W. (eds.), Singapore, **1985**, p 19.

[103] Sole, K. C.; Hiskey, J. B. *Hydrometallurgy* **1992**, *30*, 345.

[104] Hoshi, H.; Tsuyoshi, A.; Akiba, K. *J. Radioanal. Nucl. Chem.* **2000**, *243*, 621.

[105] Modolo, G.; Odoj, R. *Solvent Extr. Ion Exch.* **1999**, *17*, 33.

[106] Jensen, M. P.; Bond, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 9870.

[107] Drew, M. G. B.; Hudson, M. J.; Iveson, P. B.; Russell, M. L.; Liljenzin, J. O.; Skalberg, M.; Spjuth, L.; Madic, C. *J. Chem. Soc., Dalton Trans.* **1998**, 2973.

[108] Drew, M. G. B.; Iveson, P. B.; Hudson, M. J.; Liljenzin, J. O.; Spjuth, L.; Cordier, P. Y.; Enarsson, A.; Hill, C.; Madic, C. *J. Chem. Soc., Dalton Trans.* **2000**, 821.

[109] Cordier, P. Y.; Hill, C.; Baron, P.; Madic, C.; Hudson, M. J.; Liljenzin, J. O. *J. Alloys Compd.* **1998**, *271*, 738.

[110] Kolarik, Z.; Mullich, U.; Gassner, F. *Solvent Extr. Ion Exch.* **1999**, *17*, 23.

[111] Kolarik, Z.; Mullich, U.; Gassner, F. *Solvent Extr. Ion Exch.* **1999**, *17*, 1155.

[112] Kolarik, Z. *Solvent Extr. Ion Exch.* **2003**, *21*, 381.

[113] Hudson, M. J.; Drew, M. G. B.; Guillaneux, D.; Russell, M. L.; Iveson, P. B.; Madic, C. *Inorg. Chem. Commun.* **2001**, *4*, 12.

[114] Berthet, J. C.; Miquel, Y.; Iveson, P. B.; Nierlich, M.; Thuery, P.; Madic, C.; Ephritikhine, M. *J. Chem. Soc., Dalton Trans.* **2002**, 3265.

[115] Iveson, P. B.; Riviere, C.; Guillaneux, D.; Nierlich, M.; Thuery, P.; Ephritikhine, M.; Madic, C. *Chem. Commun.* **2001**, 1512.

[116] Madic, C.; Lecomte, M.; Baron, P.; Boulis, B. C. R. *Phys.* **2002**, *3*, 797.

[117] Hudson, M. J.; Drew, M. G. B.; Foreman, M. R. S.; Hill, C.; Huet, N.; Madic, C.; Youngs, T. G. A. *Dalton Trans*. **2003**, 1675.

[118] Drew, M. G. B.; Hill, C.; Hudson, M. J.; Iveson, P. B.; Madic, C.; Vaillant, L.; Youngs, T. G. A. *New. J. Chem*. **2004**, *28*, 462.

[119] Andersson, S.; Ekberg, C.; Foreman, M. R. S.; Hudson, M. J.; Liljenzin, J. O.; Nilsson, M.; Skarnemark, G.; Spahiu, K. *Solvent Extr. Ion Exch*. **2003**, *21*, 621.

[120] Nigond, L.; Condamines, N.; Cordier, P. Y.; Livet, J.; Madic, C.; Cuillerdier, C.; Musikas, C. *Sep. Sci. Technol.* **1995**, *30*, 2075.

[121] Kwon, S. G.; Lee, E. H.; Yoo, J. H.; Park, H. S.; Kim, J. S. *J. Kor. Nucl. Soc*. **1999**, *31*, 498.

[122] Arnaud-Neu, F.; Böhmer, V.; Dozol, J. F.; Grüttner, C.; 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.

[123] Arnaud-Neu, F.; Barboso, S.; Byrne, D.; Charbonniere, L. J.; Schwing-Weill, M. J.; Ulrich, G. *Calixarenes for Separations*, A.C.S., Symposium Series n° 757, Lumetta, G. J.; Rogers, R. D.; Gopalan, A. S.; **2000**, chapter 12, p 150.

[124] Barboso, S.; Garcia Carrera, A.; Matthews, S. E.; Arnaud-Neu, F.; Böhmer, V.; Dozol, J. F.; Rouquette, H.; Schwing-Weill, M. J. *J. Chem. Soc., Perkin Trans. 2* **1999**, 719.

[125] Lambert, T. N.; Jarvinen, G. D.; Gopalan, A. S. *Tetrahedron Lett*. **1999**, *40*, 1613.

[126] Delmau, L. H.; Simon, N.; Schwing-Weil, M. J.; Arnaud-Neu, F.; Dozol, J. F.; Eymard, S.; Tournois, B.; Böhmer, V.; Grüttner, C.; Musigmann, C.; Tunayar, A. *Chem. Commun*. **1998**, 1627.

[127] Arduini, A.; Böhmer, V.; Delmau, L.; Desreux, J. F.; Dozol, J. F.; Garcia Carrera, A.; Lambert, B.; Musigmann, C.; Pochini, A.; Shivanyuk, A.; Ugozzoli, F. *Chem. Eur. J.* **2000**, *6*, 2135.

[128] Schmidt, C.; Saadioui, M.; Böhmer, V.; Host, V.; Spirlet, M. R.; Desreux, J. F.; Brisach, F.; Arnaud-Neu, F.; Dozol, J. F. *Org. Biomol. Chem.* **2003**, *1*, 4089.

[129] Boerrigter, H.; Verboom, W.; Reinhoudt, D. N. *J. Org. Chem*. **1997**, *62*, 7148.

[130] Peters, M. W.; Werner, E. J.; Scott, M. J. *Inorg. Chem*. **2002**, *41*, 1707.

[131] Dunga, N. T. K.; Kunogi, K.; Ludwig, R. *Solvent Extraction for the 21st Century*, Cox, M.; Hidalgo, M.; Valiente, M. (eds.), London, UK, **2001**, p 249.

[132] Froidevaux, P.; Harrowfield, J. M.; Sobolev, A. N. *Inorg. Chem*. **2000**, *39*, 4678.

[133] Ludwig, R.; Kunogi, K.; Dung, N.; Tachimori, S. *Chem. Commun*. **1997**, 1985.

Chapter 3

CMP(O)/*N*-acyl(thio)urea Tetrafunctionalized Cavitands: Synthesis and Liquid-Liquid Extractions[*]

The synthesis of different carbamoylmethylphosphonate (CMP), -phosphine oxide CMPO and N-*acyl(thio)urea -tetrafunctionalized cavitands is described. Liquid-liquid extractions were performed from aqueous nitric acid into dichloromethane or* o-*nitrophenyl hexyl ether (NPHE). The extraction of americium (III) and europium (III) from aqueous nitric acid into NPHE was studied in both the absence and presence of the hexabrominated cobalt bis(dicarbollide) anion (*Br_6*-COSAN) as a synergist. CMP(O) cavitands are more efficient extractants than the corresponding* N-*acyl(thio)urea derivatives, whereas the latter show an interesting selectivity for americium (III) over europium (III) in the presence of* Br_6*-COSAN. The introduction of a propyl chain between the cavitand platform and the chelating groups increases the extraction efficiency of the ionophores **12**, **14**, and **15**. A high selectivity was achieved by* N-*acylthiourea cavitand **12** at pH 3 using* Br_6*-COSAN as a synergist.*

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[*] Reinoso-García, M. M.; Verboom, W.; Reinhoudt, D. N.; Brisach, F.; Arnaud-Neu, F.; Liger, K. *Solv. Extr. Ion Exch.*, submitted for publication.

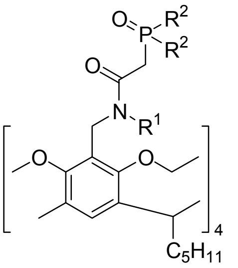
3.1 Introduction

In the literature many examples are known of preorganization of ligating sites on a molecular platform, giving rise to improved complexation properties. Appropriately functionalized calix[4]arenes[1,2] (four phenolic rings connected by methylene bridges) are being used for the complexation of alkali and alkaline earth metal ions and to a lesser extent heavy and transition metal ions.[3] In contrast to the calix[4]arenes, there are only few examples of cavitand-based receptors for cations.[4] Cavitands[5] are macrocyclic compounds of which the four aromatic rings are interconnected twice, which makes them much more rigid than the corresponding calix[4]arenes. Attachment of ligating sites to the rigid cavitand frame allows, in principle, a tight preorganization of the coordination 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.[5]

The separation of trivalent actinides from lantanides remains a challenging problem because of their close similarity, similar ionic radii and co-ordination behavior. This is especially the case if Am^{3+} has to be separated from Eu^{3+} by extraction from strongly acidic media, as it is required in the reprocessing of nuclear fuels.[6] Nevertheless, actinides have a stronger coordinative bonding with soft donor atoms such as nitrogen, sulfur, or phosphorus than lanthanides; therefore the separation is favored by the presence of soft donor atoms.[7]

Three octyl(phenyl)-*N*,*N*-diisobutylcarbamoylmethylphosphine oxide (CMPO) molecules are necessary for the coordination of a metal ion.[8] However, it was proven that when they are attached to a platform, for example a calix[4]arene,[9,10] actinides were extracted with higher efficiencies and selectivities than with the monomeric CMPO, which is used in the so-called “TRUEX”-process (see Chapter 2). The attachment of CMPOs to a cavitand has been done in our group a few years ago (Chart 3.1).[11] These molecules are very efficient as Eu^{3+} chelating agents, but no experiments with Ac^{3+} have been performed.

N-acylthioureas have sulfur, nitrogen, and oxygen as donor atoms, allowing them to act as monodentate sulfur donors, bidentate oxygen and sulfur donors, or oxygen and nitrogen donors. They can also coordinate through the keto- or enol-thione form, depending on the ligands, the metal ions, and counter anions present.[12] For this reason, *N*-acylthiourea moieties, which have already been known for a long time as metal chelating agents,[13] were selected as ligating groups. They are very useful for the removal of heavy metal cations[14] from waste water[15] and as selective extractants for separation[16] and concentration of precious metal cations such as Pd^{2+} and Pt^{2+}.[17] The soft donor character of *N*-acylthioureas makes them possible candidates for actinide/lanthanide complexation.



	R^1	R^2
1	R^1=H	R^2=Ph
2	propyl	Ph
3	H	OEt
4	propyl	OEt

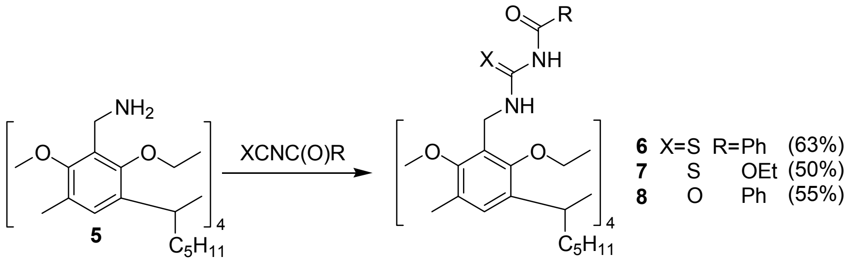
Chart 3.1. CMP(O) tetrafunctionalized cavitands.

This Chapter deals with the synthesis of CMP(O) functionalized cavitands having a propyl spacer between the molecular platform and the ligating sites. The effect of the introduction of a spacer, and consequently flexibility of the ligating sites, on the complexation behavior (liquid-liquid extraction) was studied.

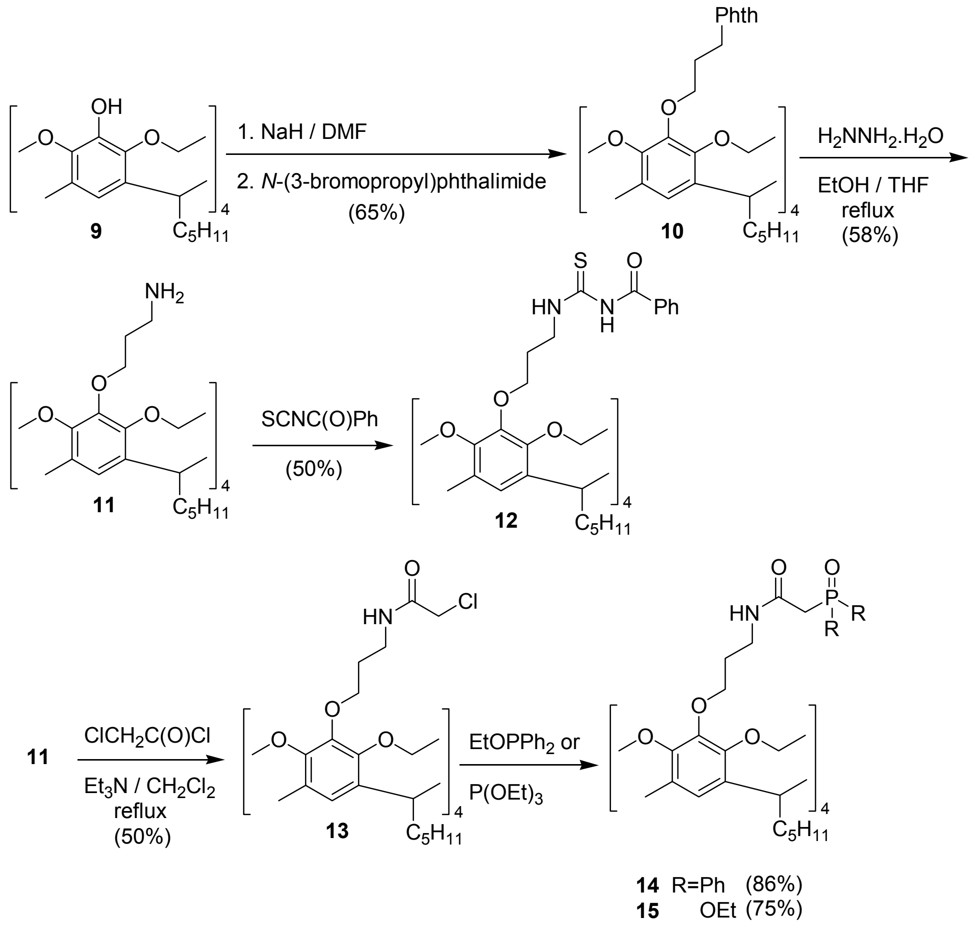
In addition, the synthesis and complexation behavior (Am^{3+}, Eu^{3+} liquid/liquid extraction) of *N*-acyl(thio)urea-tetrafunctionalized cavitands, both with short and long spacer, were investigated.

3.2 Synthesis

Cavitands **1**, **2**, **3**, and **4** were synthesized via a procedure reported by our group.[11] *N*-acyl(thio)urea cavitands **6**, **7**, and **8** were prepared from **5**[11] and benzoyl isothiocyanate, ethoxycarbonyl isothiocyanate, or benzoyl isocyanate in 63%, 50%, and 55% yield, respectively (Scheme 3.1).



Scheme 3.1.



Scheme 3.2.

In order to study the influence of a longer spacer between the platform and the ligating site, tetrahydroxycavitand[18] **9** was reacted with *N*-(3-bromopropyl)-phthalimide in the presence of NaH as a base in DMF to give tetrakis[(phthalimido)propoxy]cavitand **10** in 65% yield. Subsequent removal of the phthalimido groups with hydrazine hydrate and reaction of the resulting tetrakis(aminopropoxy)cavitand **11** with benzoyl isothiocyanate gave cavitand **12** in 50% yield (Scheme 3.2). In the ^{1}H NMR spectrum the methylene group adjacent to the nitrogen shifts from δ 3.25 in **11** to δ 3.93 in **12**. Reaction of **11** with chloroacetyl chloride and Et_3N as a base gave cavitand **13** in 50% yield (Scheme 3.2). In the ^{1}H NMR spectrum a new signal appears at δ 4.07 which belongs to the $-CH_2Cl$ group and the methylene group adjacent to the nitrogen shifts from δ 3.25 in **11** to δ 3.56 in **13**. The Arbusov reaction of cavitand **13** with ethyl diphenylphosphinite and triethylphosphite gave the target compounds **14** and **15** in 86% and 75% yield, respectively. The introduction of ligating sites was clearly confirmed from the mass spectra and satisfactory elemental analyses. The ^{1}H NMR spectra of **14** and **15** exhibit a characteristic doublet for the CH_2P hydrogens around 3 ppm.

The model compounds used, *viz*. **16** and **17** were prepared by literature procedures.[19,20]

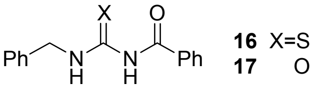


Chart 3.2. *N*-acyl(thio)urea model compounds.

3.3 Extractions

3.3.1 Extraction of Lanthanides and Thorium

In our group Boerrigter et al.[11] have found that the CMP(O) cavitands **1**-**4** show a reasonable to good affinity for Eu^{3+} in extraction studies with radiotracers at pH 3. However, actinides have not been studied. Therefore, we investigated in more detail the complexation behavior of **1**-**4** and **14** towards different lanthanides, *viz*. Eu^{3+}, La^{3+}, and

Yb^{3+}, and towards Th^{4+} since it has similar complexation properties as Pu^{4+}. The results of the extractions are summarized in Table 3.1.

The cavitands **1**-**4** and **14** all show more or less the same moderate extraction behavior toward the lanthanides. However, except for CMP cavitand **4**, they exhibit a preference for Th^{4+}. This is contradictory to the previously obtained results in our group (vide supra). A possible explanation may be the anion used, picrate in the previous studies, while now nitrate was used.

Table 3.1. Extraction percentages %E of lanthanides and thorium nitrates from 1M HNO_3 into CH_2Cl_2 by CMPO cavitands **1**-**4**, **14** (C_M=C_L=10^{-4}M, volume organic phase / aqueous phase=1, T=20°C)[a]

Cation / Ionophore	La^{3+}	Eu^{3+}	Yb^{3+}	Th^{4+}
1	7	11	8	24
2	6	9	6	17
3	8	8	9	43
4	11	11	14	10
14	13 [b]	12 [b]	7 [b]	81

a) %E = 100% ($[M^{n+}]_{org}/[M^{n+}]_{tot}$) after extraction as determined by the Arsenazo(III) assay. Precision: $\pm\sigma_{n-1}$: 1 – 2.
b) C_L = 10^{-3}M.

In the case of the Th^{4+} extraction, cavitands **1** and **3** are better extractants than their corresponding *N*-propyl analogues **2** and **4**, respectively. This behavior has also been observed in the case of CMPO-functionalized calix[4]arenes.[21] It is striking that CMPO cavitand **14**, having a longer spacer between the platform and the CMPO moieties, shows the highest extraction for Th^{4+} (81%) compared to the other compounds. In addition, it exhibits a pronounced selectivity for Th^{4+} over lanthanide complexation. Apparently, the larger flexibility of the ligating sites in compound **14** compared to **1** gives rise to better extraction results (Th^{4+} extraction of **14** *vs* **1** = 81 *vs* 24). Unfortunately, the extraction efficiency of the corresponding CMP analogue **15** could not be measured due to solubility problems.

In addition, the extraction results of cavitand **14** reveal that it has a high affinity for Th^{4+} similar in magnitude to the reported for the CMPO-calixarene systems.[22] However, it has a low and constant affinity for lanthanides making it more selective for Th^{4+}.

3.3.2 Extraction of Americium and Europium

In order to study the efficiency of the different chelating groups, *viz.* CMP(O) and *N*-acyl(thio)ureas, under simulated nuclear waste conditions, liquid-liquid extractions were carried out with *o*-nitrophenyl hexyl ether (NPHE) as the organic phase at varying nitric acid concentrations with and without hexabrominated cobalt bis(dicarbollide) anion (Br_6-COSAN)[*] as a synergistic agent (Chart 3.3). Br_6-COSAN is a lipophilic anion that facilitates the transport of the cations to the organic phase as was found for calixarenes.[23,24]

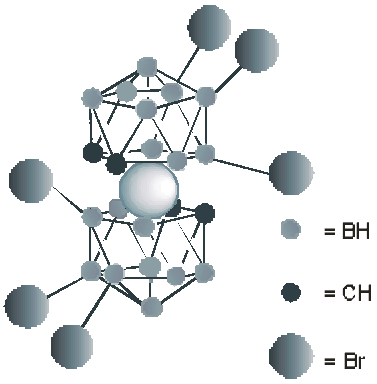


Chart 3.3. Schematic drawing of the structure of Br_6-COSAN.

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[*] For a more detailed study see Chapter 5 and references therein.

The experiments were carried out at different pH values, ranging from a 0.001M to 4M nitric acid, imposed by the need to simulate the strongly acidic conditions required in the reprocessing of nuclear waste. Americium and europium were selected due to their similarity and presence in nuclear waste.

The extraction results with compounds **1-4, 6-8**, **12**, **14-17** are summarized in Tables 3.2-3.5. The extraction data are expressed as distribution coefficients (ratio of the metal concentration in the organic phase and in the aqueous phase; see the experimental section).

3.3.2.1 CMP(O) cavitands

Table 3.2 shows that CMPO cavitands (**1** and **14**) are better ionophores than the CMP ones (**2** and **15**). This is predictable taking in account that CMPO is more basic than the CMP moieties and that CMPO-functionalized compounds should be better extractants than the CMP type reported by Horwitz *c.s.*[25] In all cases the distribution coefficients are higher for Am^{3+} than for Eu^{3+}.[22]

The introduction of longer alkyl chains modifies the extraction properties of the different ionophores. Surprisingly, CMPO cavitand **14**, only having longer spacers than **1**, has much higher distribution coefficients than **1**, especially at higher HNO_3 concentrations. Apparently, the improvement of the extraction properties comes from the higher flexibility of the ligating sites.

In order to improve the distribution coefficients and the efficiency of the CMP(O) derivatives, liquid-liquid extractions were performed with CMPO cavitand **1** as representative example and the lipophilic anion Br_6-COSAN as a synergist. The results are summarized in Table 3.3. The distribution coefficients (higher than 100 for Am^{3+} and Eu^{3+} at pH<2) show a considerable increase of the extraction efficiency. However, this increase in efficiency is not accompanied with an improvement of the selectivity.

Compared to the results obtained for the standard CMPO,[26] CMPO cavitand **1** presents higher distribution coefficients for Eu^{3+} (no measurements with Am^{3+} have been reported) in highly acidic media at lower concentrations of **1** in the presence of Br_6-COSAN (10^{-3}M and 3.10^{-3}M *vs* 10^{-2}M and 10^{-2}M).

Table 3.2. Distribution coefficients for the extraction of Eu^{3+} and Am^{3+} by CMP(O) cavitand derivatives **1**, **2**, **14**, and **15**.[a]

Ionophore	Cation	HNO$_3$ concentration (M)						
		0.001	0.01	0.1	1	2	3	4
1	Eu^{3+}	16.96	2.45	0.86	0.46	0.32	0.36	n.d.[c]
	Am^{3+}	31.33	4.34	1.35	0.57	0.67	0.83	n.d[c]
2	Eu^{3+}	5.06	10.50	10.90	0.72	0.35	0.08	0.22
	Am^{3+}	9.81	15.00	13.00	0.64	0.47	0.26	0.42
14[b]	Eu^{3+}	12.61	3.51	5.00	9.00	10.15	29.47	26.74
	Am^{3+}	31.02	7.12	10.67	28.54	21.15	28.30	63.37
15[b]	Eu^{3+}	0.05	0.03	0.35	1.30	4.14	n.d.[c]	5.31
	Am^{3+}	0.06	0.08	0.54	1.66	5.67	n.d.[c]	5.95

a)Aqueous phase: 152-Eu; 241-Am / [HNO$_3$] variable (~1500 kBq/L)/(Sp Gamma D3/0.5 mL). Organic phase: ligand (10^{-3}M) in NPHE.

b) Major precipitation at [HNO$_3$]>0.1M.

c) Not determined.

Table 3.3. Distribution coefficients for the extraction of Eu^{3+} and Am^{3+} by CMPO cavitand **1** in the presence of Br$_6$-COSAN as a synergist.[a]

Cation	HNO$_3$ concentration (M)					
	0.001	0.01	0.1	1	2	3
Eu^{3+}	>100	>100	>100	>100	2.03	1.78
Am^{3+}	>100	>100	>100	>100	3.98	3.64

a) Aqueous phase: 152- Eu; 241-Am / [HNO$_3$] variable (~1500 kBq/L)/(Sp Gamma D3/0.5 mL). Organic phase: **1** (10^{-3}M) + Br$_6$-COSAN ($3\cdot10^{-3}$M) in NPHE.

3.3.2.2. N-acyl(thio)urea cavitands

The data presented in Table 3.4 show that the *N*-acyl(thio)urea cavitands **6**-**8**, and reference compounds **16** and **17**, behave more or less in the same way, being not effective and not selective (distribution coefficients for Eu^{3+} and Am^{3+} lower than 0.001). Only compounds **7** and **16** exhibit a slight preference for Am^{3+} over Eu^{3+} at pH>2.

Table 3.4. Distribution coefficients for the extraction of Eu^{3+} and Am^{3+} by *N*-acyl(thio)urea derivatives **6**, **7**, **8**, **16**, and **17**.[a]

Ionophore	Cation	HNO_3 concentration (M)						
		0.001	0.01	0.1	1[c]	2[c]	3[c]	4[c]
6[b]	Eu^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
	Am^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
7[b]	Eu^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
	Am^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	0.0015	0.005	0.005	0.006
8	Eu^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
	Am^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
12	Eu^{3+}	n.d.[d]	n.d.[d]	$<10^{-3}$	$<10^{-3}$	n.d.[d]	n.d.[d]	$<10^{-3}$
	Am^{3+}	n.d.[d]	n.d.[d]	0.0011	0.0035	n.d.[d]	n.d.[d]	0.001
16	Eu^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
	Am^{3+}	0.002	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	0.0025	0.0036	0.01
17[b]	Eu^{3+}	$<10^{-3}$	n.d.[d]	n.d.[d]	$<10^{-3}$	n.d.[d]	$<10^{-3}$	n.d.[d]
	Am^{3+}	$<10^{-3}$	n.d.[d]	n.d.[d]	$<10^{-3}$	n.d.[d]	$<10^{-3}$	n.d.[d]

a) Aqueous phase: 152-Eu; 241-Am / [HNO_3] variable (~1500 kBq/L)/(Sp Gamma D3/0.5 mL)
Organic phase: ligand (10^{-3}M) in NPHE.
b) Major precipitation at [HNO_3]>0.1M.
c) Precipitation at [HNO_3]>1M.
d) Not determined.

However, addition of the lipophilic anion Br_6-COSAN results in a huge improvement of the extraction properties of **6**, **7**, **8**, **12**, **16**, and **17** at HNO_3 concentrations lower than 0.1M (Table 3.5). The synergistic effect is reflected in a different way, depending on the moieties that are attached to the platform. Whereas at pH>2 the *N*-acylurea derivatives (**8** and **17**) are very effective, the *N*-acylthioureas (**6** and **12**) are selective for Am^{3+}. The improvement of the efficiency can be explained by the strong pH dependence of *N*-acylthioureas;[27] at low pH they are protonated and loose their chelating properties.

Table 3.5. Distribution coefficients for the extraction of Eu^{3+} and Am^{3+} by *N*-acyl(thio)urea derivatives **6**, **7**, **8**, **12**, and **17** in the presence of Br_6-COSAN as a synergist.[a]

Ionophore	Cation	HNO_3 concentration (M)						
		0.001	0.01	0.1	1	2	3	4
6[b]	Eu^{3+}	28.30	0.13	0.27	0.03	0.03	n.d.[d]	0.04
	Am^{3+}	47.67	0.14	0.33	0.02	0.03	n.d.[d]	0.03
7[b]	Eu^{3+}	29.78	$<10^{-3}$	0.12	0.04	0.03	n.d.[d]	0.03
	Am^{3+}	38.60	0.04	0.13	$<10^{-3}$	$<10^{-3}$	n.d.[d]	$<10^{-3}$
8	Eu^{3+}	>100	>100	0.47	0.002	<0.001	n.d.[d]	n.d.[d]
	Am^{3+}	>100	>100	0.79	0.002	0.001	n.d.[d]	n.d.[d]
12[b]	Eu^{3+}	13.71	4.11	0.69	0.03	0.03	0.03	0.01
	Am^{3+}	53.33	10.76	0.84	$<10^{-3}$	0.07	$<10^{-3}$	$<10^{-3}$
16	Eu^{3+}	35.2	0.482	0.0148	0.0060	0.0046	0.0035	n.d.[d]
	Am^{3+}	57.2	0.643	0.0169	0.0035	0.0036	0.0126	n.d.[d]
17[c]	Eu^{3+}	96.32	>100	0.86	0.003	<0.001	n.d.[d]	n.d.[d]
	Am^{3+}	>100	>100	1.39	0.006	<0.001	n.d.[d]	n.d.[d]

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

b) Major precipitation at [HNO_3]>0.1M.

c) Ligand **17** 10^{-2}M.

d) Not determined.

3.4 Conclusions

CMP(O)-functionalized cavitands (**1**, **2**, **14**, and **15**) are much better extractants for Am^{3+} and Eu^{3+} than the corresponding *N*-acyl(thio)urea derivatives (**6**, **7**, **8**, **12**, **16**, and **17**) (see Tables 3.2 and 3.4). Especially CMPO cavitands (**1**, **2**, and **14**) show distribution coefficients higher than 1 in the pH range used. Despite the presence of soft donor atoms, the *N*-acyl(thio)urea cavitands (**6**, **7**, **8**, **12**, **16**, and **17**) do not have the expected affinity for lanthanides and actinides; they barely extract them (Table 3.4).

However, addition of Br_6-COSAN, a lipophilic anion that works as a synergist, to the organic phase changes the properties of these ionophores considerably (Tables 3.3 and 3.5). CMPO cavitand **1** (taken as representative example of the CMP(O) cavitands) becomes highly efficient at HNO_3 concentrations lower than 1M. *N*-acylurea cavitand **8** which almost did not have any affinity towards Eu^{3+} and Am^{3+}, did show now an unexpected affinity for them, with distribution coefficients higher than 97 at HNO_3 concentrations lower than 0.1M. The extraction efficiency of *N*-acylthiourea cavitands **6**, **7**, and **12** is also considerably increased by addition of Br_6-COSAN, but more importantly, they present higher distribution coefficients for Am^{3+} than for Eu^{3+}, which makes them suitable for actinide/lanthanide separation.

The introduction of a propyl spacer between the platform and the ligating site improves the extraction properties as was demonstrated by comparing the behavior of cavitands **12** and **14** with **6** and **1**, respectively.

3.5 Experimental section

General

^1H and ^{13}C NMR spectra were recorded on a Varian Unity INOVA (300 MHz) and a Varian Unity 400 WB NMR spectrometer, respectively. Residual solvent protons were used as an internal standard and chemical shifts are given in ppm relative to tetramethylsilane (TMS). Fast atom bombardment (FAB) mass spectra were measured on a Finnigan MAT 90 spectrometer using *m*-nitrobenzyl alcohol (NBA) as a matrix. Matrix-Assisted Laser Desorption Ionisation Time-of-Flight (MALDI-TOF) mass spectra were recorded using a

Perkin Elmer/PerSpective Biosystems Voyager-DE-RP MALDI-TOF mass spectrometer. Elemental analyses were carried out using a 1106 Carlo-Erba Strumentazione element analyser. 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. Melting points (uncorrected) of all compounds were obtained on a Reichert melting point apparatus.

Compounds **1**, **2**, **3**, **4**, **5**[11], and **11**[18] have been prepared according to literature procedures.

Tetrakis[(benzoylthiourea)methyl]cavitand 6

A solution of tetrakis(aminomethyl)cavitand **5** (100 mg, 0.107 mmol) and benzoyl isothiocyanate (121 mg, 0.744 mmol) in chloroform (10 mL) was stirred overnight at room temperature. The solution was washed with H_2O (2 × 20 mL) and dried over $MgSO_4$. The solvent was removed in vacuo and the crude product was purified by flash chromatography (SiO_2, CH_2Cl_2/hexanes 3/2) to yield **6** as a yellowish solid. Yield 107 mg (63%); mp 157-159°C; FAB-MS: *m/z* 1585.3 ($[M+H]^+$, calcd 1585.6); ^{1}H NMR ($CDCl_3$) δ 8.91 (s, 4H, NH), 7.70 (d, 8H, *J*=7.2 Hz, ArH), 7.51 (t, 4H, *J*=7.2 Hz, ArH), 7.35-7.42 (m, 8H, ArH), 7.09 (s, 4H, Ar), 6.05 (d, 4H, *J*=7.5 Hz, OCH_2O), 4.72-4.77 (m, 12H, ArCHAr, $ArCH_2NH$), 4.10 (d, 4H, *J*=7.5 Hz, OCH_2O), 2.01-2.10 (m, 8H, CH_2), 1.21-1.34 (m, 24H, CH_2), 0.85 (t, 12H, *J*=6.6 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 178.9, 166.1, 133.0, 153.3, 137.8, 131.2, 128.6, 128.1, 126.9, 119.9, 99.8, 39.9, 36.4, 31.6, 29,7, 29.2, 27.1, 22.1, 13.6; Anal. calcd for $C_{88}H_{96}N_8O_{12}S_4$: C, 66.64; H, 6.10; N, 7.07; S, 8.09. Found: C, 66.61; H, 5.99; N, 6.94; S, 7.95.

Tetrakis[(ethoxycarbonylthioureido)methyl]cavitand 7

A solution of tetrakis(aminomethyl)cavitand **5** (150 mg, 0.16 mmol) and ethoxycarbonyl isothiocyanate (0.23 mL, 0.48 mmol) in acetonitrile (10 mL) was stirred overnight at room temperature. The white precipitate was filtered off and dried in vacuo to afford **7**. Yield 160 mg (50%); mp 143-146°C; FAB-MS: *m/z* 1457.0 ($[M+H]^+$, calcd 1457.0); ^{1}H NMR ($CDCl_3$) δ 9.86 (s, 4H, CH_2NHCO), 7.93 (s, 4H, CSNHCO), 7.05 (s, 4H, ArH), 6.01 (d, 4H,

J=7.3 Hz, OCH_2O), 4.75-4.80 (m, 12H, ArCHAr, $ArCH_2NH$), 4.41 (d, 4H, J=7.3 Hz, OCH_2O), 4.21 (q, 8H, J=7.3 Hz, OCH_2), 2.18-2.23 (m, 8H, CH_2), 1.27-1.45 (m, 36H, CH_2+CH_3), 0.94 (t, 12H, J=6.2 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 176.8, 151.8, 150.5, 136.3, 120.0, 118.4, 98.4, 61.0, 38.4, 30.1, 28.2, 20.7, 12.3, 12.2; Anal. calcd for $C_{72}H_{96}N_8O_{16}S_4$: C, 59.32; H, 6.64; N, 7.69; S, 8.80. Found: C, 59.16; H, 6.51; N, 7.75; S, 8.75.

Tetrakis[(benzoylurea)methyl]cavitand 8

A solution of tetrakis(aminomethyl)cavitand **5** (200 mg, 0.858 mmol) and benzoyl isocyanate (555 mg, 3.77 mmol) in THF (20 mL) was refluxed overnight. The reaction mixture was evaporated to dryness and redissolved in CH_2Cl_2 (20 mL). The solution was washed with H_2O (100 mL) and subsequently dried over $MgSO_4$. Evaporation of the solvent gave a yellowish solid which was recrystallized two times from diethyl ether giving a white solid. Yield 180 mg (55%); mp 137-139°C; MALDI-MS: *m/z* 1544.6 ($[M+Na]^+$, calcd 1544.8); ^1H NMR ($CDCl_3$) δ 8.93 (s, 4H, NH), 7.78 (d, 8H, J=6.9 Hz, ArH), 7.51-7.64 (m, 4H, ArH), 7.39-7.48 (m, 8H, ArH), 7.03 (s, 4H, ArH), 6.01 (d, 4H, J=7.8 Hz, OCH_2O), 4.82 (t, 4H, J=8.1 Hz, ArCHAr), 4.42 (d, 4H, J=7.8 Hz, OCH_2O), 4.25 (s, 8H, $ArCH_2NH$), 2.18-2.23 (m, 8H, CH_2), 1.31-1.49 (m, 24H, CH_2), 0.93 (t, 12H, J=6.6 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 207.2, 154.9, 153.5, 138.2, 133.7, 131.4, 129.2, 128.9, 128.2, 127.7, 65.8, 36.8, 32.1, 30.1, 27.6, 22.7, 15,3, 14.1; Anal. calcd for $C_{88}H_{92}N_8O_{16}$: C, 69.64; H, 6.11; N, 7.38. Found: C, 70.01; H, 6.23; N, 7.41.

Tetrakis(phthalimidopropoxy)cavitand 10

A suspension of tetrol **9** (500 mg, 0.57 mmol) and NaH (219 mg, 9.12 mmol) in dry DMF (50 mL) was heated for 30 min at 65°C. Subsequently, bromopropylphthalimide (3 g, 11.4 mmol) was added and heating was continued for 3 days at 90°C. After removal of the solvent, the residue was dissolved in EtOAc (25 mL), and 1N HCl was added till pH 7. The solution was washed with water (3 × 25 mL) and brine (1 × 25 mL) and dried over $MgSO_4$. Evaporation of the solvent gave a brown oil, which was further purified by flash chromatography (SiO_2, EtOAc/hexanes, 1:2) to afford pure **10** as a white solid. Yield 373 mg (65%); mp 150-153°C; FAB-MS: *m/z* 1629.7 ($[M+H]^+$, calcd 1629.3); ^1H NMR

($CDCl_3$) δ 7.82-7.86 and 7.69-7.73 (2m, 8+8H, ArH), 6.79 (s, 4H, ArH), 5.90 (d, 4H, *J*=7.0 Hz, OCH_2O), 4.70 (t, 4H, *J*=8.0 Hz, ArCHAr), 4.43 (d, 4H, *J*=7.0 Hz, OCH_2O), 4.02 (t, 8H, *J*=5.8 Hz, OCH_2), 3.91 (t, 8H, *J*=5.4 Hz, CH_2N), 2.14-2.19 and 2.04-2.13 (2m, 8+8H, CH_2+CH_2), 1.27-1.42 (m, 24H, CH_2), 0.91 (t, 12H, *J*=6.9 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 167.7, 147.7, 143.8, 138.3, 133.3, 131.7, 122.6, 113.5, 99.0, 70.5, 36.5, 34.9, 31.6, 29.4, 28.9, 27.1, 22.1, 13.6; Anal. calcd for $C_{96}H_{100}N_4O_{20}$: C, 70.75; H, 6.18; N, 3.44. Found: C, 70.78; H, 6.40; N, 3.17.

Tetrakis(aminopropoxy)cavitand 11

A solution of **10** (608 mg, 0.38 mmol) and hydrazine hydrate (247 mg, 7.7 mmol) in a 9/1 mixture of EtOH/THF (30 mL) was refluxed overnight. After addition of concentrated HCl (0.5 mL) refluxing was continued for another hour. Upon cooling of the reaction mixture 2M NaOH was added till pH 10 to give a precipitate. The precipitate was filtered off and washed with H_2O (5 mL). The residue was dissolved in CH_2Cl_2 (15 mL) and the resulting solution was dried over $MgSO_4$. Evaporation of the solvent gave **11** as a white solid. Yield 248 mg (58%); mp 188-190°C; FAB-MS: *m/z* 1109.7 ($[M+H]^+$, calcd 1109.7); ^{1}H NMR ($CDCl_3$) δ 7.71-7.73 (m, 8H, NH_2), 6.69 (s, 4H, ArH), 6.18 (d, 4H, *J*=7.8 Hz, OCH_2O), 4.64 (t, 4H, *J*=8.0 Hz, ArCHAr), 4.47 (d, 4H, *J*=8.0 Hz, OCH_2O), 4.07 (t, 8H, *J*=5.1 Hz, OCH_2), 3.25-3.33 (m, 8H, CH_2N), 2.02-2.21 (m, 8+8H, CH_2+CH_2), 1.27-1.42 (m, 24H, CH_2), 0.84 (t, 12H, *J*=7.3 Hz, CH_3); Anal. calcd for $C_{64}H_{92}N_4O_{12}.3CH_2Cl_2$: C, 57.47; H, 7.34; N, 4.00. Found: C, 57.14; H, 7.10; N, 4.12.

Tetrakis[(benzoylthioureido)propoxy]cavitand 12

A solution of **11** (200 mg, 0.18 mmol) and benzoyl isothiocyanate (227.5 mg, 1.44 mmol) in chloroform (10 mL) was stirred at room temperature for 3 days. The solution was washed with H_2O (2 × 20 mL) and dried over $MgSO_4$. The solvent was removed in vacuo and the crude product was purified by flash chromatography (SiO_2, CH_2Cl_2/hexanes, 3:2) to give **12** as a yellowish solid. Yield 159 mg (50%); mp 90-92°C; FAB-MS: *m/z* 1761.5 ($[M+H]^+$, calcd 1761.7); ^{1}H NMR ($CDCl_3$) δ 9.02 (s, 4H, NH), 7.80 (d, 8H, *J*=8.1 Hz, ArH), 7.30-7.64 (m, 12H, ArH), 6.83 (s, 4H, ArH), 5.93 (d, 4H, *J*=7.2 Hz, OCH_2O), 4.74 (t, 4H, *J*= 8.4 Hz, ArCHAr), 4.50 (d, 4H, *J*=6.9 Hz, OCH_2O), 4.04 (t, 8H, *J*=5.1 Hz, OCH_2), 3.93 (q, 8H, *J*=5.4 Hz, CH_2N), 2.15-2.20 (m, 8H, CH_2), 2.08 (q, 8H, *J*=5.4 Hz, CH_2), 1.27-1.42 (m, 24H, CH_2), 0.91 (t, 12H, *J*=6.9 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 179.9, 166.8, 148.3, 144.2, 138.9, 133.4, 132.0, 129.1, 127.0, 114.3, 99.8, 71.1, 43.4, 37.0, 32.1, 29.9, 28.8, 27.7, 22.7, 14.1; Anal. calcd for $C_{96}H_{112}N_8O_{16}S_4$: C, 65.43; H, 6.41; N, 6.36; S, 7.28. Found: C, 65.60; H, 6.15; N, 6.75; S, 7.05.

Tetrakis[(chloroacetamido)propoxy]cavitand 13

To a solution of **11** (500 mg, 0.353 mmol) and Et_3N (714 mg, 7.07 mmol) in CH_2Cl_2 (25 mL) was added chloroacetyl chloride (638 mg, 5.65 mmol). The reaction mixture was refluxed overnight. The solution was washed with 1M HCl (1 × 75 mL), H_2O (2 × 50 mL), 2M NaOH (3 × 25 mL), and 1M HCl (2 × 25 mL) and dried over $MgSO_4$. The solvent was removed in vacuo to give **13** as a brownish foam. Yield 159 mg (50%); FAB-MS: *m/z* 1415.0 ($[M+H]^+$, calcd 1414.8); ^1H NMR ($CDCl_3$) δ 7.05 (t, 4H, J=5.5 Hz, NH), 6.83 (s, 4H, ArH), 5.84 (d, 4H, J=6.9 Hz, OCH_2O), 4.71 (t, 4H, *J*=8.0 Hz, ArCHAr), 4.41 (d, 4H, *J*=7.3 Hz, OCH_2O), 4.07 (s, 8H, CH_2Cl), 3.99 (t, 8H, *J*=5.5 Hz, OCH_2), 3.56 (q, 8H, *J*=6.2 Hz, CH_2N), 2.09-2.20 (m, 8H, CH_2), 1.91 (q, 8H, *J*=6.2 Hz, CH_2), 1.27-1.42 (m, 24H, CH_2), 0.91 (t, 12H, *J*=6.2 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 166.1, 154.5, 148.2, 144.2, 139.0, 114.4, 62.5, 42.7, 36.9, 32.0, 27.6, 22.6, 14.1; Anal. calcd for $C_{72}H_{96}Cl_4N_4O_{16}.H_2O$: C, 60.33; H, 6.89; N, 3.91. Found: 60.35; H, 6.74; N, 3.68.

Tetrakis[(diphenyl-N-methylcarbamoylmethylphophineoxide)propoxy]cavitand 14

In an open flask compound **13** (250 mg, 0.184 mmol) was dissolved in a small amount of ethyl diphenylphosphinite (2 mL) while the temperature was gradually increased from 100°C to 150°C, and the mixture was stirred for 1 h at 150°C. After cooling of the reaction mixture diisopropyl ether was added till a precipitate was formed. The precipitate was filtered off and the brown solid was further purified by column chromatography (Sephadex LH-20, MeOH/CH_2Cl_2, 1/1) to give **14** as a slightly brown solid. Yield 332 mg (86%); mp 131-133°C; FAB-MS: *m/z* 2077.1 ($[M+H]^+$, calcd 2077.8); ^1H NMR ($CDCl_3$) δ 7.70-7.8 and 7.41-7.47 (2m, 16+24H, P-phenyl), 6.82 (s, 4H, ArH), 5.80 (d, 4H, *J*=7.3 Hz, OCH_2O), 4.71 (t, 4H, *J*=8.0 Hz, ArCHAr), 4.34 (d, 4H, *J*=7.3 Hz, OCH_2O), 3.79 (t, 8H, *J*=5.5 Hz, OCH_2), 3.24-3.40 (m, 8+8H, P-CH_2+CH_2N), 2.14-2.28 (m, 8H, CH_2), 2.08 (q, 8H, *J*=5.5 Hz, CH_2), 1.31-1.46 (m, 24H, CH_2), 0.91 (t, 12H, *J*=6.9 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 164.2, 147.6, 143.7, 138.3, 131.7, 130.3, 128.3, 128.2, 113.5, 99.0, 70.4, 38.7, 37.9, 36.4, 31.5, 29.4, 27.7, 22.1, 13.6; Anal. calcd for $C_{120}H_{136}N_4O_{20}P_4.4CH_2Cl_2$: C, 69.35; H, 6.60; N, 2.70. Found: C, 69.27; H, 6.58; N, 2.51.

Tetrakis[(diethyl-N-methylcarbamoylmethylphosphate)propoxy]cavitand 15

In an open flask compound **13** (320 mg, 0.23 mmol) was dissolved in a small amount of triethyl phosphite (3 mL) while the temperature was gradually increased from 100°C to 150°C, and the mixture was stirred for 1 h at 150°C. After cooling of the reaction mixture, diisopropyl ether was added till a precipitate was formed. The precipitate was filtered off and thoroughly washed with diisopropyl ether, and subsequently purified by column chromatography (Sephadex LH-20, MeOH/CH_2Cl_2, 1/1) to give **15** as a brownish solid. Yield 326 mg (78%); mp 108-110°C; FAB-MS: *m/z* 1843.9 ($[M+Na]^+$, calcd 1843.8); ^{1}H NMR ($CDCl_3$) δ 7.05 (t, 4H, *J*=5.5 Hz, NH), 6.83 (s, 4H, ArH), 5.85 (d, 4H, *J*=7.3 Hz, OCH_2O), 4.70 (t, 4H, *J*=8.4 Hz, ArCHAr), 4.37 (d, 4H, *J*=7.0 Hz, OCH_2O), 4.11- (m, 16H, OCH_2CH_3), 3.99 (t, 8H, *J*=6.5 Hz, OCH_2), 3.56 (q, 8H, *J*=6.2 Hz, CH_2N), 2.87 (d, 8H, *J*=21.8 Hz, CH_2P), 2.09-2.20 (m, 8H, CH_2), 1.89-1.91 (m, 8H, CH_2), 1.27-1.42 (m, 24H, CH_2), 0.91-1.15 (m, 24+12H, OCH_2CH_3+CH_3); ^{13}C NMR ($CDCl_3$) δ 166.1, 148.2, 144.2, 139.0, 114.4, 99.6, 62.7, 42.7, 36.9, 32.0, 29.9, 27.6, 22.7, 16.3, 14.1; Anal. calcd for $C_{88}H_{136}N_4O_{28}P_4.5CH_2Cl_2$: C, 49.72; H, 6.55; N, 2.49. Found: C, 49.40; H, 6.41; N, 2.64.

Extraction of Ln^{3+} and Th^{4+}

The aqueous phase consisted of solutions of lanthanide or thorium nitrates (10^{-4}M) in 1M HNO_3 and the organic phase of solutions of the cavitands **1**-**4** and **14** in dichloromethane (10^{-4}-10^{-3}M). 1 mL of each phase was put in a stoppered tube and stirred at 20°C for 12 h. After separation of the layers, the aqueous phase was monitored spectrophotometrically using Arsenazo (III) (2,2’-[1,8-dihydroxy-3,6-disulfonaphthalene-2,7-diylbis(azo)] bis(benzenarsonic acid)) as colored reagent. The Arsenazo solution was prepared by dissolving the reagent in a sodium formate-formic acid buffer (pH=2.8). 5 mL of this solution (6.4×10^{-4}M) were then added to a 0.65 mL aliquot of the aqueous phase and the volume adjusted to 50 mL with the buffer. The absorbances A were determinated at 665 nm for Th^{4+} and 655 nm for Ln^{3+}. Since the concentration of Arsenazo is 30 times higher than the concentration of the cations, complete complexation can be assumed. The percentage of cation extracted was calculated as:

$$\%E = \frac{[A_1 - A]}{[A_1 - A_0]} \times 100$$

where A_0 is the absorbance of the Arsenazo solution without the cation and A_1 the absorbance of the Arsenazo solution containing the known concentration of the cation before extraction.

Liquid –liquid extractions of Eu^{3+} and Am^{3+}

The aqueous phase was chosen to simulate real occurring waste solutions. An aqueous phase was prepared at varying concentrations of nitric acid (0.01-4M). Europium, as radioisotope ^{152}Eu, and americium, as radioisotope ^{241}Am, were added at an activity around 1500 kBq dm^{-3}, which corresponds approximatively 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 (**1**, **2**, **6-8**, **12**, **14-17**) 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 $\sum[M_{org}]$ and $\sum[M_{aq}]$ denote the total concentration of the metal species in the organic and in the aqueous phase, respectively:

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

3.6 References

[1] Talanova, G.; Elkarim, N. S. A.; Talanov, V. S.; Bartsch, R. A. *Anal. Chem.* **1999**, *71*, 3106.

[2] Arena, G.; Contino, A.; Longo, E.; Sciotto, D.; Sgarlata, C.; Spoto, G. *Tetrahedron Lett.* **2003**, *29*, 5415.

[3] Wieser, C.; Dieleman, C. B.; Matt, D. *Coord. Chem. Rev.* **1997**, *165*, 93.

[4] Boerrigter, H.; Verboom, W.; Reinhoudt, D. N. *Liebigs Ann./Recueil* **1997**, 2247.

[5] Verboom, W. *Cavitands* in *Calixarenes 2001*, Asfari, Z.; Böhmer, V.; Harrowfield, J.; Vicens, J. (eds.), Kluwer Academic Publishers, Dordrecht, **2001**, p 181.

[6] Horwitz, E. P.; Kalina, D. G.; Diamond, H.; Vandergrift, D. G.; Schultz, W. W. *Solvent Extr. Ion Exch.* **1985**, *3*, 75.

[7] Jensen, M. P.; Nash, K. L. *Solvent Extraction for the 21st Century*, Cox, M.; Hidalgo, M.; Valiente, M. (eds.), London, UK, **2001**, p 1089.

[8] Horwitz, E. P.; Diamond, H.; Martin, K. A.; Chiarizia, R. *Solvent Extr. Ion Exch.* **1987**, *5*, 419.

[9] Arnaud-Neu, F.; Böhmer, V.; Dozol, J. F.; Gruttner, C.; 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.

[10] Peters, M. W.; Werner, E. J.; Scott, M. J. *Inorg. Chem*. **2002**, *41*, 1707.

[11] Boerrigter, H.; Verboom, W.; Reinhoudt, D. N. *J. Org. Chem*. **1997**, *62*, 7148.

[12] Yuan, Y. F.; Wang, J. T.; Gimeno, M. C.; Laguna, A.; Jones, P. G. *Inorg. Chim. Acta* **2001**, *324*, 301 and references cited therein.

[13] Siedler, J. *J. Prakt. Chem*. **1880**, *21*, 140.

[14] Druzilla, M. *Inorg. Chim. Acta* **1991**, *181*, 85.

[15] (a) Schwarzer, M.; Schuster, M. *Anal. Chim. Acta* **1996**, *328*, 1; (b) Ringmann, S.; Schuster, M. *Chem. Tech*. **1997**, *49*, 217; (c) Sandor, M. Geistmann, F.; Schuster, M. *Anal. Chim. Acta* **2003**, *486*, 11.

[16] El Aamrani, F. Z.; Kumar, A.; Cortina, J. L.; Saster, A. M. *Anal. Chim. Acta* **1999**, *382*, 205.

[17] Koch, K. R. *Coord. Chem. Rev*. **2001**, *216-217*, 473.

[18] Irwin, J. L.; Sherburn, M. S. *J. Org. Chem*. **2000**, *65*, 5846.

[19] Van der Groot, H.; Schepers, M. J. P.; Sterk, G. J.; Timmerman, H. *Eur. J. Med. Chem. Chim. Ther.* **1992**, *5*, 517.

[20] Nakagawa, Y.; Wheelock, C. E.; Morisseau, C.; Goodrow, M. H.; Hammock, B. G.; Hammock, B. D. *Bioorg. Med. Chem*. **2000**, *8*, 2663.

[21] Schmidt, C.; Saadioui, M.; Böhmer, V.; Host, V.; Spirlet, M. R.; Desreux, J. F.; Brisach, F.; Arnaud-Neu, F.; Dozol, J. F. *Org. Biomol. Chem.* **2003**, *1*, 4089.

[22] Barboso, S.; Carrera, A. G.; Matthews, S. E.; Arnaud-Neu, F.; Böhmer, V.; Dozol, J. F.; Rouquette, H.; Schwing-Weill, M. J. *J. Chem. Soc., Perkin Trans. 2* **1999**, 719.

[23] Kyrš, M.; Svoboda, K.; Lhoták, P.; Alexová, J. *J. Radioanal. Nucl. Chem.* **2002**, *254,* 455.

[24] Kyrš, M.; Svoboda, K.; Lhoták, P.; Alexová, J. *J. Radioanal. Nucl. Chem.* **2003**, *258,* 497.

[25] Kalina, D. G.; Horwitz, E. P.; Kaplan, L.; Muscatello, A. C. *Sep. Sci. Technol.* **1981**, *16*, 1127.

[26] Grüner, B.; Plešek, J.; Báča, J.; Císařová, I.; Dozol, J. F.; Rouquette, H.; Viñas, C.; Selucký, P.; Rais, J. *New J. Chem.* **2002**, *26*, 1519.

[27] Ringmann, S.; Schuster, M. *Chem. Tech.* **1997**, *49*, 217.

Chapter 4

Potentiometric Studies of Complexation Properties of Tetrafunctionalized Cavitands*

The binding properties of different carbamoylmethylphosphonate (CMP), -phosphine oxide (CMPO) and N-*acyl(thio)urea tetrafunctionalized cavitands towards different cations are described. Extraction studies with metal (Pb^{2+}, Cu^{2+}, Ag^{+}, Hg^{2+}, Cd^{2+}, Eu^{3+}, Fe^{3+}, K^{+}, Na^{+}, and Ca^{2+}) picrates and the incorporation in ion selective electrodes (ISEs), show that there is more than a 40% increase of the Ag^{+} extraction for* N-*acylthiourea ionophores (**2**, **3**, and **8**) in comparison with* N-*benzoyl-*N'-*benzylthiourea (**9**). CMP(O) cavitands (**1**, **2**, **3**, **4**, **9**, and **10**) form very stable complexes ($\log \beta_{ML} > 18$) for most of the examined cations as determined with the segmented sandwich method. Potentiometric studies with the corresponding ion selective electrodes revealed that while cavitands functionalized with CMP(O) moieties (**1**, **2**, **3**, **4**, **9**, and **10**) exhibit the highest selectivity for UO_2^{2+} and Pb^{2+} and a pronounced discrimination of Ag^{+} ions,* N-*acyl(thio)urea derivatives (**5**, **6**, **7**, **8**, **11**, and **12**) show preferences for Ag^{+} and Pb^{2+} and a reduced selectivity toward UO_2^{2+}. Stoichiometry studies showed for* N-*acylthiourea derivative a ligand:metal ratio of 1:1, while for the corresponding model compound **11** a ratio of 1:2 was found.*

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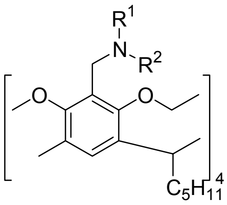
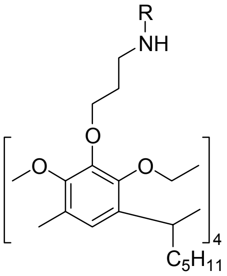
4.1 Introduction

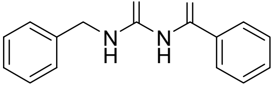
In Chapter 3, CMP(O)- and *N*-acyl(thio)urea-tetrafunctionalized cavitands were used as ionophores in liquid-liquid extractions of actinides and lanthanides. However, no studies towards other cations were performed. In this Chapter the complexation, extraction, and sensing behavior of these ionophores (Chart 4.1) toward representatives of various other cations (*e.g.*, Ag^+, Na^+, K^+, Pb^{2+}, Cd^{2+}, Hg^{2+}, Mg^{2+}, Ca^{2+}, Cu^{2+}, Sr^{2+}, UO_2^{2+}, and Fe^{3+}) will be described.



	R^1	R^2
1	R^1=$C(O)CH_2P(O)Ph_2$	R^2=H
2	$C(O)CH_2P(O)Ph_2$	C_3H_7
3	$C(O)CH_2P(O)(OCH_2CH_3)$	H
4	$C(O)CH_2P(O)(OCH_2CH_3)$	C_3H_7
5	$C(S)NH_2C(O)Ph$	H
6	$C(S)NH_2C(O)OCH_2CH_3$	H
7	$C(O)NH_2C(O)Ph$	H



8 R=$C(S)NHC(O)Ph$
9 $C(O)CH_2P(O)Ph_2$
10 $C(O)CH_2P(O)(OCH_2CH_3)_2$



11 X=S
12 O

Chart 4.1.

4.2 Liquid-Liquid extractions

For the *N*-acyl(thio)urea derivatives **5**, **6**, **7**, **8**, **11**, and **12** the extractions were done according to the standard picrate extraction method.[1] The results, expressed as a percentage of extracted cation (%E), are summarized graphically in Figure 4.1.

All tetrafunctionalized compounds exhibit high extraction values for Ag^+, especially the *N*-acylthiourea derivatives **5**, **6**, and **8**. The extraction levels are higher than those observed for other sulphur-containing calix[4]arene-based ionophores.[2] Moreover, ionophores **5**, **6**, and **8** display high Ag^+/Pb^{2+} selectivities: $S_{Ag+/Pb2+}$ = 26.3, 42.4, and 52.6, respectively, in comparison with values of 11.4 and 8.1 reported for *p-tert*-butyldihomooxacalix[4]arene and a *p-tert*-butylcalix[4]arene with phenylketones as ligating sites, respectively.[3]

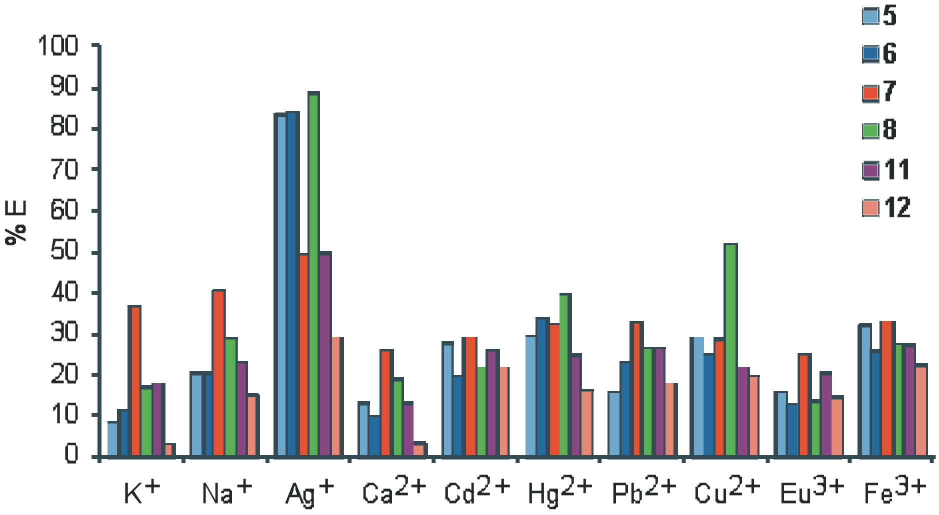


Figure 4.1. Extraction results of *N*-acyl(thio)urea derivatives **5**, **6**, **7**, **8**, **11**, and **12**.

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

Surprisingly, both tetrakis[(benzoylthioureido)methyl]cavitand **5** and the corresponding model compound **11** have more or less the same extraction profile. However, tetrakis[(benzoylthioureido)propoxy]cavitand **8**, only having a longer spacer than **5**, is able to extract twice the amount of Cu^{2+} than **5** (29%) and model compound **11** (22%). It is striking that **8** extracts two times more Hg^{2+} than Cd^{2+}, since these cations have a similar ionic radius.[4] Apparently, the slightly improved extraction properties come from the higher flexibility of the ligating sites, rather than the preorganization. In the case of tetrakis[(benzoylureido)methyl]cavitand **7** preorganization clearly plays a role in the complexation of the alkali and alkaline earth metal ions as follows from comparison of the data of **7** and model compound **12**. Model compound **12** shows almost no extraction of K^+ (3%) and Ca^{2+} (4%), and only 15% of Na^+ was extracted, whereas **7** is able to extract K^+ (37%), Na^+ (41%), and Ca^{2+} (26%) in substantially higher percentages. However, in general, **7** extracts all the other cations more or less to the same extent.

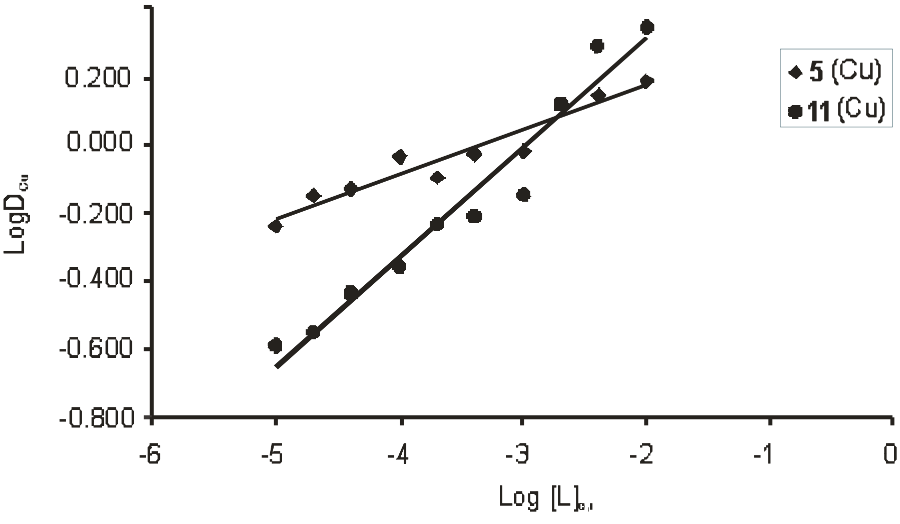


Figure 4.2. Plots of log D_{Cu}^{2+} *vs* log $[L]_{o,i}$ of **5** and **11**.

Conditions: $[Cu^{2+}]_{w,i}=10^{-4}M$; $[LiPic]_w=10^{-3}M$; pH=3.

The stoichiometry coefficient p was determined using equation (1) taking into account that only one complex is present and that the metal is unassociated in the aqueous phase.

$$LogD = logK_{ex} + nlog[Pic^{-}]_{aq} + plog[L]_{org} \tag{1}$$

The representation of log D *vs* log [L] should be linear with a slope of p, where p indicates the number of ligand molecules involved per cation in the extracted species.

Plots of log D *vs* log [L] for the extraction of Cu^{2+} by tetrakis[(benzoylthiourea)methyl] cavitand **5** and model compound **11** are given in Figure 4.2. For the complexation of **5** with Cu^{2+} the plots are linear with slopes close to one, in agreement with the formation of 1:1 complexes. In the case of model compound **11** the slope is close to 2 indicating the formation of 1:2 complexes, which is in agreement with the reported complexation behavior.[5] The same stoichiometries were obtained for Pb^{2+}.

4.3 Potentiometric studies

Synthetic receptors have been successfully used as ion-carriers (ionophores) in the membranes of ion-selective electrodes (ISEs). Although thousands of various ionophores have already been designed and synthesized,[6] still there is a need for more selective ionophores, especially now that the feasibility of a decrease of the detection limit has recently been shown.[7] Therefore the interaction of different cations (Ag^{+}, K^{+}, Na^{+}, UO_2^{2+}, Pb^{2+}, Hg^{2+}, Ca^{2+}, Cd^{2+}, Sr^{2+}, Cu^{2+}, Mg^{2+}, and Eu^{3+}) with ionophores **1-12** was investigated.

The response of ISEs to ions can be described by the empirical Nicolsky–Eisenman equation (2):

$$EMF = E_i^0 + (RT/z_iF)ln(a_i + \sum K_{i,j}^{pot} a_j^{z_i/z_j}) \tag{2}$$

where a_i is the analyte ion activity, a_j is the interfering ion activity, z_i and z_j are the charges of analyte and interfering ions, respectively and the symbols R, T, and F have their usual meaning. The selectivity coefficient, $K_{i,j}^{pot}$, describes the ability of an electrode to recognize an analyte ion (i) in the presence of interfering ions (j). When the value of $\log K_{i,j}^{pot}$ is smaller than 0, it means that the electrode is more selective to the primary ion than to interfering ions.[8] 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 ion-ionophore complexes in the membrane and the membrane concentrations of the ionophore and ionic sites.[9,10] However, the main factor that is primarily responsible for the selectivity of polymeric membrane electrodes is the selectivity of ion–ionophore interactions that can be expressed by relative stability constants of complexes formed by an ionophore with primary and interfering ions within the membrane phase.

Several methods allowing the measurement of formal ion–ionophore complex formation constants in solvent polymeric membrane phases have been proposed.[11–16] The sandwich membrane methods[10,13,12] seem to be the most appropriate for the characterization of the chemical properties of lipophilic ligands by potentiometry, since other methods suffer from drawbacks related to requirements for an additional reference (*e.g.*, chromoionophore,[13] pH ionophore,[14,15] or a lipophilic cation (TMA^+)[16]). The sandwich membrane consists of two membranes attached one to another. One of these membranes contains ionophore and ion-exchanger and the second membrane is ionophore free, with the other constituents the same. The electrode with sandwich membrane, assembled just prior to the measurement, is immersed into the sample solution of composition identical to that of the internal electrolyte of the electrode. The resulting initial membrane potential reflects the ion activity ratio at both aqueous phase-membrane interfaces (equation 3):[17]

$$E_{mem} = \frac{RT}{z_i F} ln \frac{a_i(org)''}{a_i(org)'} \qquad (3)$$

where a_i(org)’ is the ion activity at the sample–membrane interface and a_i(org)” is the ion activity at the interfilling electrolyte membrane interface. Due to specific interaction of the tested ion with the ionophore, the activity of uncomplexed ion is decreased at the ionophore-containing side of the sandwich membrane, compared to the ionophore-free side. This decrease, related to the strength of ion–ionophore interaction, is responsible for the measured potential of the electrode and used to calculate the ion–ionophore complex stability constant.

4.3.1 Complex stability constants

For both the *N*-acyl(thio)urea and CMP(O) derivatives (Chart 4.1) the complex formation constants were determined by means of the segmented sandwich method.[12]

The different ligating groups allow the quantitative investigation of the influence of the donor atoms' basicity on the complexation capability of the functionalized cavitands. The different spacer lenghts allow study of the effect of the introduction of flexibility on the complexation. According to Pearson's theory,[18] the P=O group is a hard Lewis base and can preferably interact with hard Lewis acids. The replacement of phosphine oxide/phosphate by amide/thioamide groups might lead to receptors, with complexation properties shifted toward soft metal cations. Compounds **5**, **6**, **8**, and **11** possess softer ligating groups than the P=O group: C=O and C=S, and therefore they are expected to form preferentially complexes with soft metal cations.

The experiments for the determination of complex formation constants were carried out for membranes containing potassium tetrakis[3,4-bis(trifluoromethyl)phenyl]borate (KTFPB) as lipophilic anionic sites and *o*-nitrophenyl octyl ether (*o*-NPOE) as a plasticizer in order to minimize the effects of ion-pairing and the cation-platicizer interaction competitive to the ionophore, respectively, that might affect the binding constants.[19]

4.3.1.1 CMP(O)-functionalized cavitands

Table 4.1 shows that the logarithmic values of complex formation constants for CMP(O) containing ionophores **1**, **2**, **3**, **4**, **9**, and **10** range from 31.0 to 5.3 and essentially they follow the order: Eu^{3+} >> UO_2^{2+} > Pb^{2+}, Cu^{2+}, Cd^{2+}, Sr^{2+} > Ca^{2+}, Mg^{2+} >> Ag^+, K^+, Na^+. The high values of the complex stability constants for Eu^{3+} and UO_2^{2+} confirm that these cavitands are strong receptors for these cations.

Table 4.1. Formal complex formation constants, log β_{ML} obtained with CMP(O) and *N*-acyl(thio)urea derivatives (**1-11**) in PVC/*o*-NPOE (1:2) membranes, using the segmented sandwich method.

Ionophore / Cation	CMP(O)						*N*-acyl(thio)urea				
	1	**2**	**3**	**4**	**9**	**10**	**5**	**6**	**7**	**8**	**11**
Eu^{3+}	27.6	24.7	31.0	28.1	27.7	22.5	10.6	n.d.[a]	5.2	n.d.[a]	n.d.[a]
UO_2^{2+}	22.4	18.7	25.5	20.3	22.6	17.7	5.4	10.3	6.1	8.9	8.4
Pb^{2+}	18.8	16.0	22.5	18.2	18.3	12.7	8.9	11.6	5.6	11.4	8.8
Cd^{2+}	18.1	15.6	22.7	16.7	16.8	13.4	n.d.[a]	11.8	5.9	9.8	7.4
Sr^{2+}	18.5	13.7	21.4	n.d.[a]	15.2	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]
Cu^{2+}	17.4	15.9	21.7	17.7	17.0	13.8	8.1	12.4	4.5	(18.4)	11.3
Ag^{+}	6.4	5.3	8.9	7.5	7.4	5.5	7.2	10.1	3.2	8.0	6.4
Ca^{2+}	14.0	12.7	16.9	n.d.[a]	16.6	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]
Mg^{2+}	14.4	11.4	16.5	n.d.[a]	14.4	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]
K^{+}	6.7	5.6	10.2	n.d.[a]	5.6	n.d.[a]	<2	n.d.[a]	<3	n.d.[a]	n.d.[a]
Na^{+}	7.2	7.2	12.0	8.0	7.6	6.1	4.9	4.9	4.2	4.4	5.3

a) Not determined.

The values of log β_{ML} for the phosphonate-functionalized cavitands **3** and **4** are larger than those for the phosphine oxide ones (**1** and **2**). This indicates that the phosphonate derivatives have stronger complexation properties than the phosphine oxide ones. These results are surprising, since it has been reported that the complexation properties of P-containing compounds follow the order: phosphonate < phosphate < phosphine oxide, when alkyl chains are present at those groups.[20,21] However, it has also been shown that phenyl substituents decrease the basicity of a P=O group.[22] This is very likely the explanation for the lower β_{ML} values measured for phenyl phosphine oxide-functionalized cavitands **1** and **2** compared to the ethylphosphate-functionalized ones (**3** and **4**). Moreover, the geometry of the substituents (Ph- *vs* EtO-) might also affect the architecture of the cavity of the cavitand

and, as a consequence, the complexing properties. Cavitand derivatives with a propyl spacer between the platform and the ionophore (**9** and **10**), follow the expected trend of complexation, phosphine oxide > phosphonate.

4.3.1.2 N-*acyl(thio)urea- functionalized cavitands*

For the *N*-acyl(thio)urea-functionalized cavitands **5**, **6**, **7**, and **8** as well as for the model compound **11**, much lower values, ranging from 11.8 to below 3 (with an exception for Cu^{2+}) were obtained (Table 4.1). The complex formation constants β_{ML} for these ionophores follow the order: $Pb^{2+} > UO_2^{2+}$, Cu^{2+}, $Cd^{2+} > Ca^{2+}$, $Mg^{2+} > Ag^{+} > K^{+}$, Na^{+}. The complex formation constants are generally lower for the *N*-acylurea ionophore **7** than for the *N*-acylthiourea ones **5**, **6**, **8**, and **11**.

It can be noted that the *N*-acylthiourea ionophores **5**, **6**, **8**, and **11** have a relatively higher affinity for Cu^{2+} than for the other cations, especially **8**, which has a complexation constant of 18.4.

Ethoxycarbonylthioureacavitand **6** forms slightly stronger complexes than benzoylthioureacavitand **5** with most of the examined cations. This can be explained by the fact that ethoxycarbonyl moieties interact stronger than phenylcarbonyl groups with hard and soft Lewis acids.[23] In addition, the ethoxy substituents are smaller and more flexible than the –C(O)Ph moieties.[24]

The complex formation constants, log β_{ML}, for **8** with Pb^{2+} and especially Cu^{2+} are significantly larger than those for **5** (Table 4.1). This indicates that the presence of a longer spacer ($-C_3H_6-$ in **8** *vs* $-CH_2-$ in **5**) might create a better architecture of the cavity for complexation of these cations. However, the value of log β_{CuL} is given in brackets and should be treated as an approximation. This is due to the fact that the reproducibility of the potential measurements was much worse than in other cases ($\Delta\log \beta_{CuL} \leq \pm 1.3$) and, as mentioned above, electrodes with membranes doped with **8** did not exhibit a linear response to the logarithm of the Cu^{2+} activity in sample solutions.

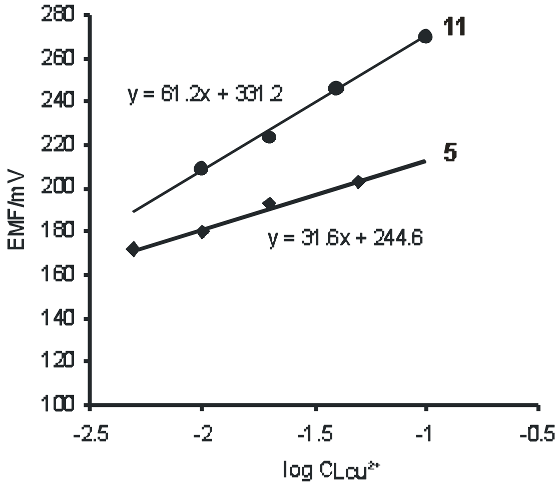


Figure 4.3. Dependence of the sandwich membrane electrodes' potential values on the content of ionophores **5** and **11**.

For tetrakis[(benzoylthiourea)methyl]cavitand **5** and model compound **11**, additional membranes with different amounts of the ionophore (5-100 mmol/kg) and constant content of anionic additives (1 mmol/kg) were prepared in order to check the stoichiometry of the complexes formed with chosen cations (Cu^{2+} and Pb^{2+}). The results obtained for Cu^{2+} are illustrated in Figure 4.3. The linear relationships between the EMF and logarithmic values of free ionophore concentration suggest that one type of complexes is predominant in the membrane.[30] The slope of the regression line close to 30 mV indicates a 1:1 **5**-Cu^{2+}complexation, while in the case of **11**-Cu^{2+} a complexation with 1:2 stoichiometry can be expected (the slope is close to 60 mV). The same behavior was found in the case of Pb^{2+}.

4.3.2 Potentiometric response to cations and membranes selectivity

All compounds (**1**-**12**) were studied as ionophores in *o*-NPOE/PVC membranes. Their potentiometric selectivity was investigated. To obtain unbiased $K_{i,j}^{pot}$ values, the calibrations for cations were collected starting from the most discriminated ones.[5,25] The order in which the cations were examined for each ionophore was established after the preliminary screening of the electrode selectivities. The electrodes exhibited a Nernstian or near-Nernstian cationic response in pure solutions of the moderately and highly discriminated ions, at least within the range 10^{-3} - 10^{-1}M. When a flattening (or a reversing) of the calibration curves was observed, the selectivity coefficients were obtained from the Nernstian portion of the response curve at lower activities.

Diagrams of the logarithmic values of the selectivity coefficients calculated for Pb^{2+} as the primary cation (log $K_{Pb,j}^{pot}$) are presented in Figures 4.4 and 4.5. As seen from these diagrams, all the examinated compounds induce a selectivity that differs from the Hofmeister selectivity pattern, observed for membranes based on a typical ion-exchanger (see last column in Figures 4.4 and 4.5) and related to the free energy of hydration of the cations.[5]

4.3.2.1 CMP(O)-functionalized cavitands

Compounds **1**, **2**, and **9** (CMPO derivatives) and **3**, **4**, and **10** (CMP derivatives) used as ionophores within the polymeric membrane, exhibit a high selectivity towards UO_2^{2+} and Pb^{2+} ions (Figure 4.4). The values of the selectivity coefficients log K_{Pb,UO_2}^{pot} for all CMPO and CMP cavitands range from +2.3 to +1.3 indicating a better selectivity towards UO_2^{2+} than for Pb^{2+} ions. Pronounced interferences ($\log K_{Pb,M}^{pot}$ ranging from –1 to –2.5) were observed for Ca^{2+}, Cd^{2+}, Cu^{2+}, and Ag^{+}. Essentially, the selectivity pattern shown in Figure 4.4 reflects the complexation capability of P-containing cavitands described by their complex stability constants (see Table 4.1). It should be pointed out that the selectivity for Pb^{2+} over Ag^{+} ions for membranes based on **1** and **3** was found to be much better than reported for tri-*n*-octylphosphine oxide[26] and calixarene phosphine oxides[27] investigated in *o*-NPOE/PVC membranes. The values of the selectivity coefficients ($\log K_{Pb,Ag}^{pot}$) for membranes with those phosphine oxides were at least three logarithmic units lower than obtained for membranes doped with **1** and **3**. The strongest discrimination was observed for alkali metal ions (Na^{+}, K^{+}). At this point it should be noted that the values of the selectivity coefficients for Na^+ and K^+ cations should be treated as approximate and overestimated due to a sub-Nernstian reponse (40-45 mV dec^{-1} slopes) of the electrodes to these ions.

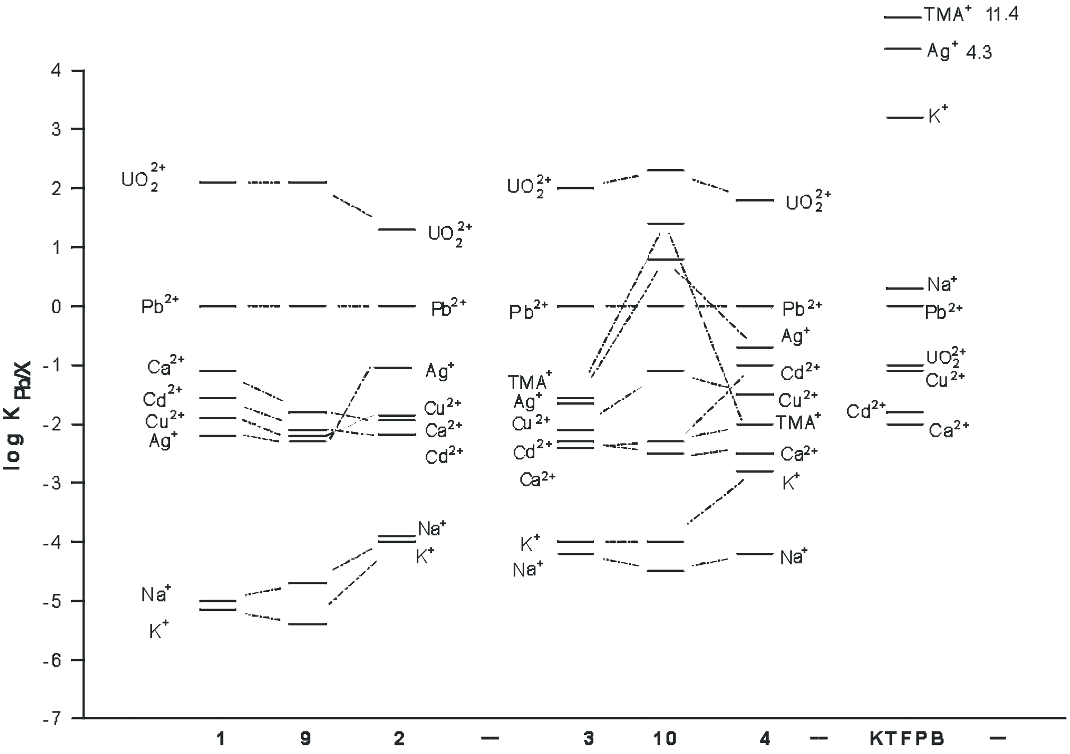


Figure 4.4. Selectivity coefficients for electrodes prepared with PVC/*o*-NPOE (1:2 by weight) membranes containing CMP(O) derivatives **1**, **2**, **3**, **4**, **9**, and **10** and lipophilic sites (KTFPB) as well as membranes with ion-exchanger only, with Pb^{2+} as the primary cation.

The incorporation of a propyl spacer between the cavitand platform and the CMPO moiety (**9**) selectivity results in a pronounced improvement of the membrane selectivity for Pb^{2+} over the divalent cations Ca^{2+}, Cu^{2+}, and Cd^{2+}. In contrast, the presence of an *N*-propyl substituent in CMPO cavitand **2** leads to a considerable loss in the membrane selectivity for

Pb^{2+} and UO_2^{2+} over Ag^+ cations and a worse selectivity over Na^+ and K^+ cations, compared to **1**. The increase of the log $K^{pot}_{Pb,TMA}$ value indicates that cavitand **2** forms much weaker complexes with Pb^{2+} than **1** and **9**. This is reflected in the complex formation constants, β_{PbL}, for **2** which are a few orders of magnitude smaller than for **1** and **9** (see Table 4.1).

The introduction of an *N*-propyl substituent in CMP cavitands gives rise to minor changes in the selectivity of the electrodes (comparison of **3** and **4**; Figure 4.4). However, the presence of a propyl spacer, compound **10**, has a much stronger influence; it exhibits weaker complexation properties than **3** and **4** (Figure 4.4). For Pb^{2+} the stability constants (log β_{PbL}) of **3** and **4** are by 9.8 and 5.5 units larger than that of **10**, respectively. The stronger ligation of Cu^{2+} than Pb^{2+} to cavitand **10** and the weaker complexation of Cu^{2+} than Pb^{2+} by **3** and **4** might explain the significant increase of log $K^{pot}_{Pb,Cu}$ for a membrane based on **10** compared to that of **3** and **4**.

4.3.2.2 N-*acyl(thio)urea-functionalized cavitands*

The amide carbonyls (and very likely thioamide thiocarbonyls as well) are known to be more weakly donating than the phosphoryl oxygens.[28,29] Soft cations are preferentially bound by ligands with a donor atom of lower electronegativity than oxygen, such as nitrogen or sulfur (electronegativity of 3.5, 3.0, and 2.5, respectively).[18] The selectivity observed for membranes doped with the *N*-acyl(thio)urea containing ionophores **5**, **6**, **7**, **8**, **11**, and **12** correlates well with these predictions and measured complex stability constants. A much better selectivity towards Ag^+ than to Pb^{2+} was observed. Also, a pronounced increase of the interference from Cu^{2+} can be seen. In contrast, the discrimination of hard UO_2^{2+} and Ca^{2+} ions is much higher than observed for CMP- or CMPO-functionalized cavitands. For *N*-acylthioureas a pronounced improvement of the membrane selectivity for Cd^{2+}, K^+, and Na^+ was achieved by incorporation of a propyl spacer (**8** *vs* **5**; Figure 4.5)

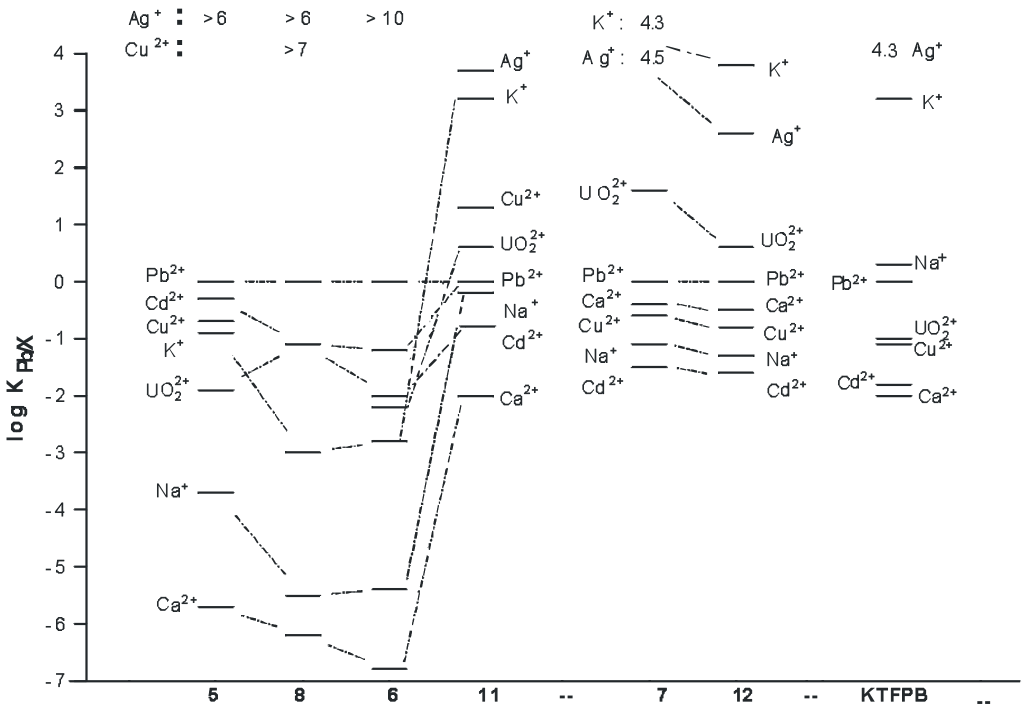


Figure 4.5. Selectivity coefficients for electrodes prepared with PVC/*o*-NPOE (1:2 by weight) membranes containing *N*-acyl(thio)urea derivatives **5**, **6**, **7**, **8**, **11**, and **12** and lipophilic sites (KTFPB) as well as membranes with ion-exchanger only, with Pb^{2+} as the primary cation.

4.4 Conclusions

Liquid-liquid extractions showed that *N*-acylthiourea tetrafunctionalized cavitands are reasonable to good ionophores for the extraction and detection of soft metal ions with a preference for Ag^+. The attachment of four *N*-acylthiourea moieties to a molecular platform clearly improves the complexation behavior. In the case of ionophores **5**, **6**, and **8** a 40% increase of the Ag^+ extraction was observed, compared with the corresponding model compound **11**. The importance of flexibility of the ligating sites clearly follows from the different complexation behavior of ionophores **5** and **8**, only differing in length of the spacer between the platform and the ligating site. The latter ionophore shows a very good affinity for Cu^{2+}.

It has been demonstrated, via potentiometric sandwich membrane measurements, that cavitands tetrafunctionalized with CMPO (**1**, **2**, and **9**) and CMP moieties (**3**, **4**, and **10**) form very strong complexes with hard cations, such as Eu^{3+} and UO_2^{2+}. The complex formation constants obtained for the other examined cations are significantly lower.

N-acyl(thio)urea tetrafunctionalized cavitands have lower complexation properties than the CMP(O) tetrafunctionalized cavitands ($\log \beta_{ML} < 10$ *vs* $\log \beta_{ML} > 10$. This can be explained by the fact that the phosphoryl oxygens are stronger donating than the amide and thioamide (thio)carbonyls.[28,29]

The selectivity coefficients obtained with ion selective electrodes correlate well with the complex stability constants. It can be concluded that CMPO- and CMP- modified cavitands (**1** and **3**) are good ionophores in membranes of UO_2^{2+}- and Pb^{2+}-selective electrodes, especially, since the discrimination of Ag^+ ions is larger than for already reported ionophores. The selectivity of electrodes with membranes based on *N*-acyl(thio)urea derivatives are less interesting in terms of preparing analytically useful ion-selective electrodes. However, the strong discrimination of Na^+ and Ca^{2+} by *N*-acylthioamide derivatives (**5**, **6**, and **8**) makes these ionophores potentially useful as a Pb^{2+} selective ionophore in the absence of significant amounts of Ag^+, Cd^{2+}, and Cu^{2+} ions in a test solution.

In the case of the *N*-acyl(thio)ureas there is a good correlation between the liquid-liquid extraction and ISE data.

4.5 Experimental section

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 10^{-3}M stock solutions of the ligands were prepared by dissolving the appropiate 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 two phases were separated 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 × 100%), defined as the ratio of the activity in the organic phase (Ao) and the total activity in both the organic and the aqueous phase (Aw), is expressed by the following equation:

$$\%E = (A_o / (A_o + A_w)) \times 100\%$$

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 (5 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 h, the resulting membrane was peeled from the glass plate and discs of 7 mm diameter were cut out.

The procedure for preparation of 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 1wt% of ionophore, and 30 mol% (relative to ionophore) 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: $Ag/AgCl_{(s)}$ / 3M KCl / bridge electrolyte / sample / ion-selective membrane / inner filling solution / $AgCl_{(s)}/Ag$. The bridge electrolyte consisted of 1M lithium acetate. The inner filling solution of the ISEs was a 0.01M solution of NaCl. The EMF values were measured using a custom made 16-channel electrode monitor. Details of this equipment have been described previously.[30]

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.[9] Selectivity coefficient $K_{i,j}^{pot}$ values were obtained from adequate, unbiased E^0 measurements for each ion, according to the equation:

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

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.[31]

Determination of stability constants

Experiments were carried out according to the procedure described in literature.[12,17] 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, $1\cdot10^{-1}$M KCl, $1\cdot10^{-2}$ M TMACl, $1\cdot10^{-2}$M $CuCl_2$, $1\cdot10^{-2}$M $SrCl_2$, $5\cdot10^{-3}$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) or $1\cdot10^{-2}$M $EuCl_3$ (pH=3)). 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, β_{iL_n}, was calculated from the following equation:

$$\beta_{iL_n} = (L_T - \frac{n}{z_i} R_T^-)^{-n} exp(\frac{z_i F}{RT} \Delta EMF)$$

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

4.6 References

[1] Moore, S. S.; Tarnowski, T. L.; Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6398.

[2] Yordanov, A. T.; Whittlesey, B. R.; Roundhill, D. M. *Inorg. Chem.* **1998**, *37*, 3526.

[3] Marcos, P. M.; Ascenso, J. R.; Segurado, M. A. P.; Pereira, J. L. C. *J. Incl. Phenom.* **2002**, *42*, 281.

[4] Marcus, Y. *Ion Properties*, Marcel Dekker: New York, **1997**, p 47.

[5] Beyer, L.; Hoyer, E.; Liebscher, J.; Hartmann, H. *Z. Chem.* **1981**, *21*, 81.

[6] Bühlmann, P.; Pretsch, E.; Bakker, E. *Chem. Rev.* **1998**, *98*, 1593.

[7] Sokalski, T.; Ceresa, A.; Zwickl, T.; Pretsch, E. *J. Am. Chem. Soc.* **1997**, *46*, 11347.

[8] Umezawa, Y.; Bühlmann, P.; Umezawa, K.; Tohda, K.; Amemiya, S. *Pure Appl. Chem.* **2000**, *72*, 1851.

[9] Bakker, E.; Pretsch, E.; Bühlman, P. *Anal. Chem.* **2000**, *72*, 1127.

[10] Bakker, E.; Bühlman P.; Pretsch, E. *Chem. Rev.* **1997**, *97*, 3083.

[11] Mokrov, S. B.; Stefanowa, O. K.; Materowa E. A.; Ivanowa, E. E. *Vestn. Leningr. Univ.* **1984**, *16*, 41.

[12] Qin, Y.; Mi, Y.; Bakker, E. *Anal. Chim. Acta* **2000**, *421*, 207.

[13] Bakker, E.; Willer, M.; Lerchi, M.; Seiler, K.; Pretsch, E. *Anal. Chem.* **1994**, *66*, 516.

[14] Bakker, E.; Pretsch, E. *Anal. Chem.* **1998**, *70*, 295.

[15] Bakker, E.; Pretsch, E. *J. Electrochem. Soc.* **1997**, *144*, L125.

[16] Ceresa, A.; Pretsch, E. *Anal. Chim. Acta* **1999**, *395*, 41.

[17] Mi, Y.; Bakker, E. *Anal. Chem.* **1999**, *395*, 41.

[18] Pearson, G. R. *J. Am. Chem. Soc.* **1963**, *85*, 353.

[19] Shultz, M. M.; Stefanowa, O. K.; Mokrow, S. B.; Mikhelson, K. N. *Anal. Chem.* **2002**, *74*, 510.

[20] Goldberg, I.; Meyerstain, D. *Anal. Chem.* **1980**, *52*, 2105.

[21] Lou, C. S.; Chang, F. C.; Yeh, Y. C. *Anal. Chem.* **1982**, *54*, 2333.

[22] Marcus, Y. *Chem. Rev.* **1963**, *63*, 139.

[23] Gutmann, V. *Coordination chemistry in non-aqueous solvents*, Springer: New York, **1971**.

[24] Stoikov, I. I.; Omran, O. A.; Solovieva, S. E.; Latypov, S. K.; Enikeev, K. M.; Gubaidullin, A. T.; Antipin, I. S.; Konovalov, A. I. *Tetrahedron* **2003**, *59*, 1469.

[25] Wygladacz, K.; Malinowska, E.; Szczygelska-Tao, J.; Biernat, J. F. *J. Inclusion Phenom.* **2001**, *39*, 303.

[26] Xu, D.; Katsu, T. *Electroanalysis* **2001**, *13*, 868.

[27] Cadogan, F.; Kane, P.; McKervey, M. A.; Diamond, D. *Anal. Chem.* **1999**, *71*, 5544.

[28] Horwitz, E. P.; Martin, K. A.; Diamond, H.; Kopalan, L. *Solv. Extr. Ion. Exch.* **1986**, *4*, 449.

[29] Cook, A. G.; Mason, G. W. J. J. *Inorg. Nucl. Chem*. **1973**, *35*, 2093.

[30] Brzózka, Z. *Pomiary Autom. Kontrola* **1988**, *9*, 197.

[31] Meier, P.C. *Anal. Chim. Acta* **1982**, *136*, 363.

Chapter 5

Cavitands Substituted with Cobalt bis(dicarbollide) Ions: Synthesis and Liquid-Liquid Extractions

*COSAN-containing cavitands functionalized at the upper rim with CMPO (**19**),* N-*acylthiourea (**20**), or picolinamide (**21**) ligating sites have better extraction properties towards Eu^{3+} and Am^{3+} than the corresponding reference cavitands (**22-24**). COSAN-containing* N-*acylthiourea cavitand **20**, which has a long and flexible spacer between the COSAN and the cavitand, has distribution coefficients about 6000 times higher than reference* N-*acylthiourea cavitand **23**. The superiority of covalently linked COSAN is clearly demonstrated in the case of* N-*acylthiourea cavitand **20** compared with synergistic mixtures of the corresponding reference cavitand **23** and added Br$_6$-COSAN.*

5.1 Introduction

Singly charged chloro derivatives of cobalt bis(dicarbollide)(1-), *closo*-[(1,2-$C_2B_9H_{11})_2$-3,3'-Co]$^-$ were designed more than 25 years ago for the extraction of $^{137}Cs^+$ from highly acidic solutions (Chart 5.1).[1,2,3] A characteristic property of these compounds is their high solubility in organic solvents, making them readily extractable from aqueous systems. This behavior is a consequence of the hydridic nature of the B-H hydrogen atoms arising from the delocalization of the negative charge over the polyhedral framework.[1] The cobalt bis(dicarbollide) is a large hydrophobic anion which exhibits the properties of a strong acid. In the extraction process, of which the modified procedure is called "UNEX",[4] Cs^+ is extracted due to the tight ion pair formation with the hexachlorinated cobalt bis(dicarbollide) anion **1** (Cl_6-COSAN), subsequently Sr^{2+} can be effectively extracted with a synergistic mixture of dicarbollide and polyethylene glycols or crown ethers. The advantage of this method is the high stability of the halogenated anion towards extreme acidity and radiation, while a disadvantage is its low solubility in apolar solvents (*e.g.* hydrocarbons).

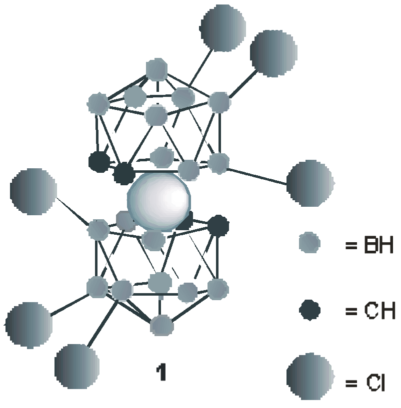


Chart 5.1. Hexachlorinated cobalt bis(dicarbollide) anion **1**.

It has been reported that the transfer of Eu^{3+} from nitric acid solutions to the organic phase could be facilitated by the presence of dicarbollide ions in the organic phase.[5,6,7] In Chapter 3, a synergistic mixture of CMP(O)- or *N*-acyl(thio)urea-tetrafunctionalized cavitands with the corresponding bromo derivative of cobalt bis(dicarbollide)(1-), *closo*-$[(1,2\text{-}C_2B_9H_{11})_2\text{-}3,3'\text{-Co}]^-$ (Br_6-COSAN) was used for the extraction of Am^{3+} and Eu^{3+} from nitric acid solutions into *o*-nitrophenyl hexyl ether (*o*-NPHE). The presence of this lipophilic anion enhanced the extraction efficiency of all the ionophores studied.

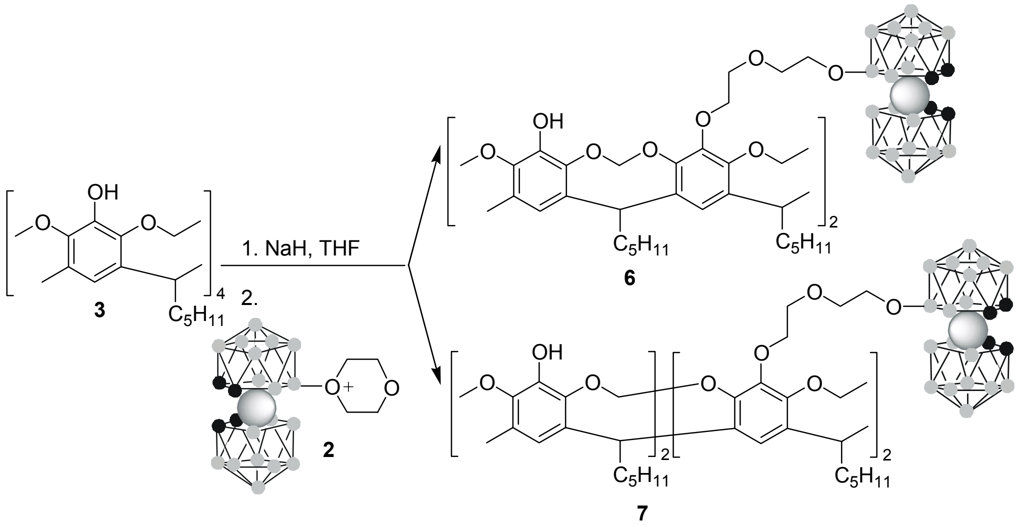
Recently, crown ethers[8] have been covalently attached to cobalt bis(dicarbollide), giving better selectivity for Cs^+ and Sr^{2+} with respect to Na^+ than the single crown ethers ($S_{Sr/Na}>10$ and >1.8, respectively, at 1M HNO_3). CMPO moieties[9] have also been covalently attached to cobalt bis(dicarbollide), giving rise to significantly better extraction efficiencies for Eu^{3+} ($D_{Eu}>100$ at 2M HNO_3) than the organic CMPO alone or synergistic mixtures of Br_6-COSAN and CMPO ($D_{Eu}=0.18$ and 15, respectively).

Thus, this Chapter deals with the synthesis and extraction properties towards Eu^{3+} and Am^{3+} of three CMPO-, *N*-acylthiourea-, and picolinamide-tetrafunctionalized cavitands containing cobalt bis(dicarbollide) ions covalently bound at the lower rim.

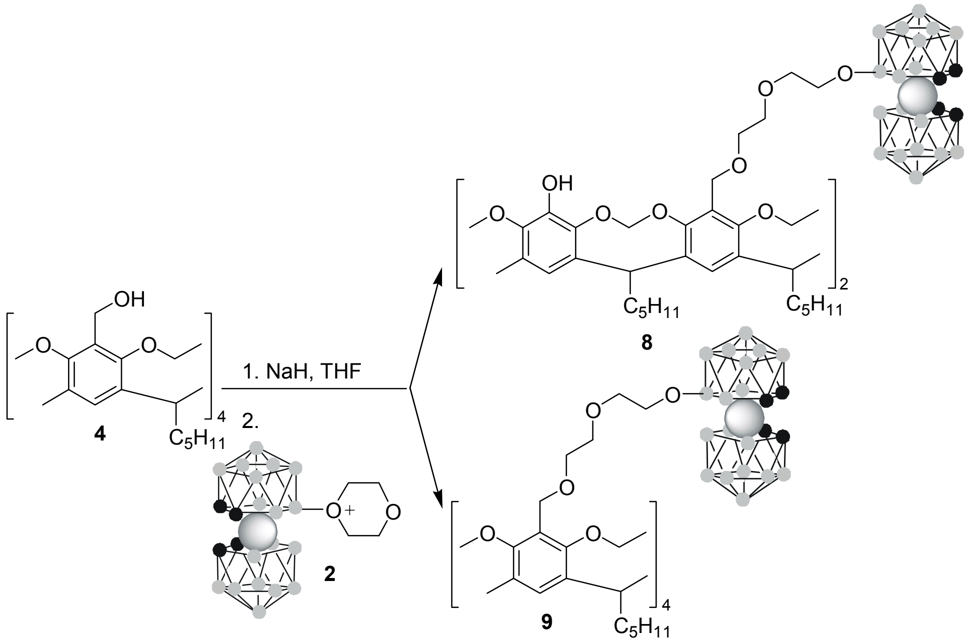
5.2 Synthesis

5.2.1 Linkage of cobalt bis(dicarbollide) ions with cavitands having different types of OH groups

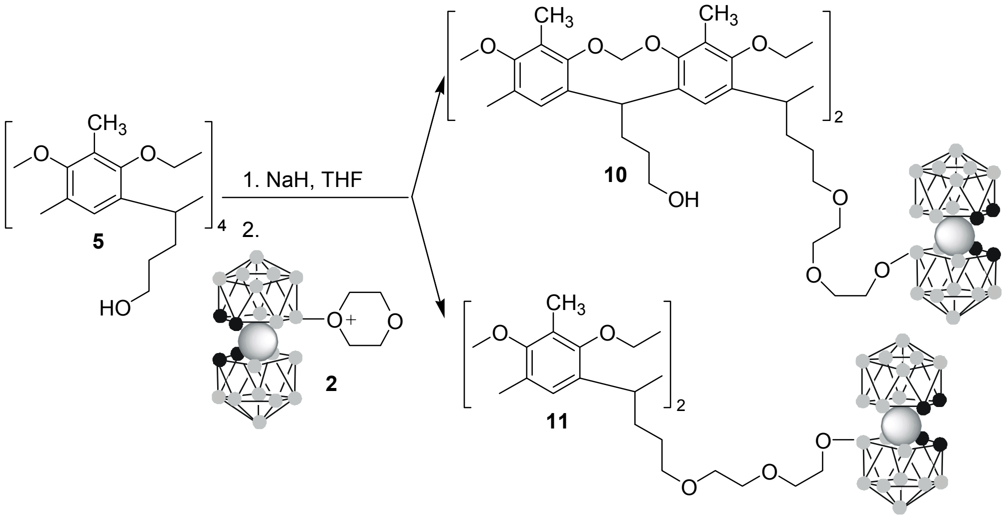
The previously described hydroxyl-containing cavitands **3**,[10] **4**,[11] and **5**[12] were used to establish a general synthetic protocol for the attachment of COSAN moieties by the group of Dr. Grüner at the Institute of Inorganic Chemistry of the Academy of Sciences (Czech Republic). Compounds **3**, **4**, and **5** were reacted with COSAN dioxane derivative (**2**)[13] giving di- and tetrasubstituted compounds as the main products, dependent on the conditions used (Schemes 5.1, 5.2, and 5.3).[14]



Scheme 5.1.



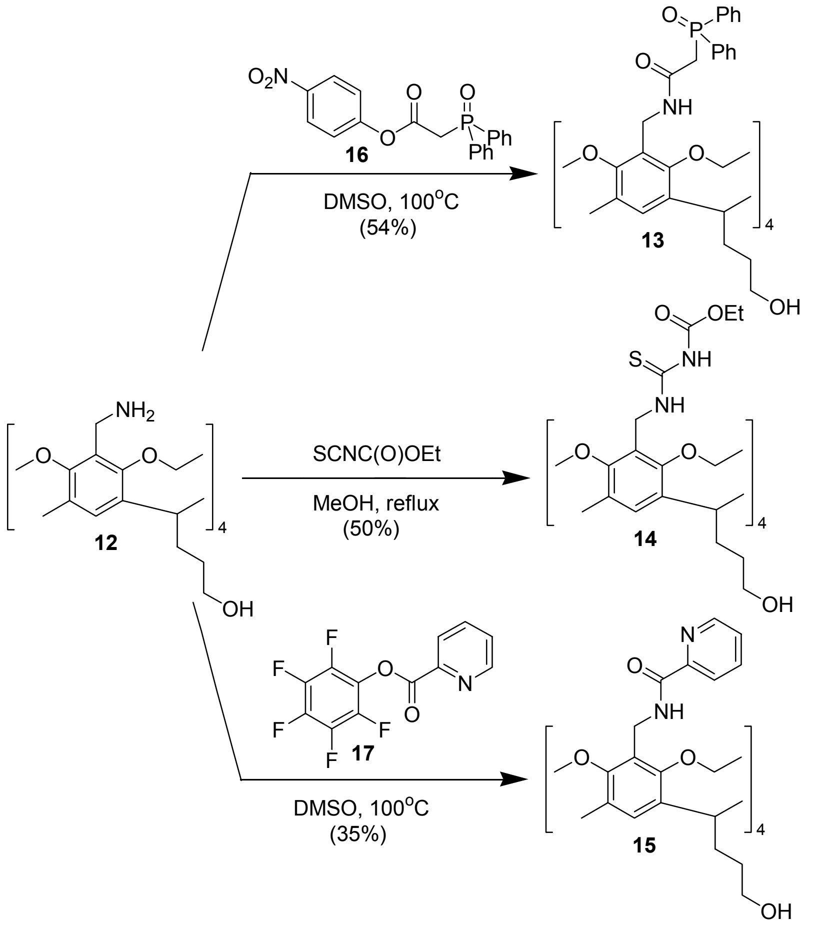
Scheme 5.2.



Scheme 5.3.

5.2.2 Appropriately functionalized cavitands covalently linked to COSAN

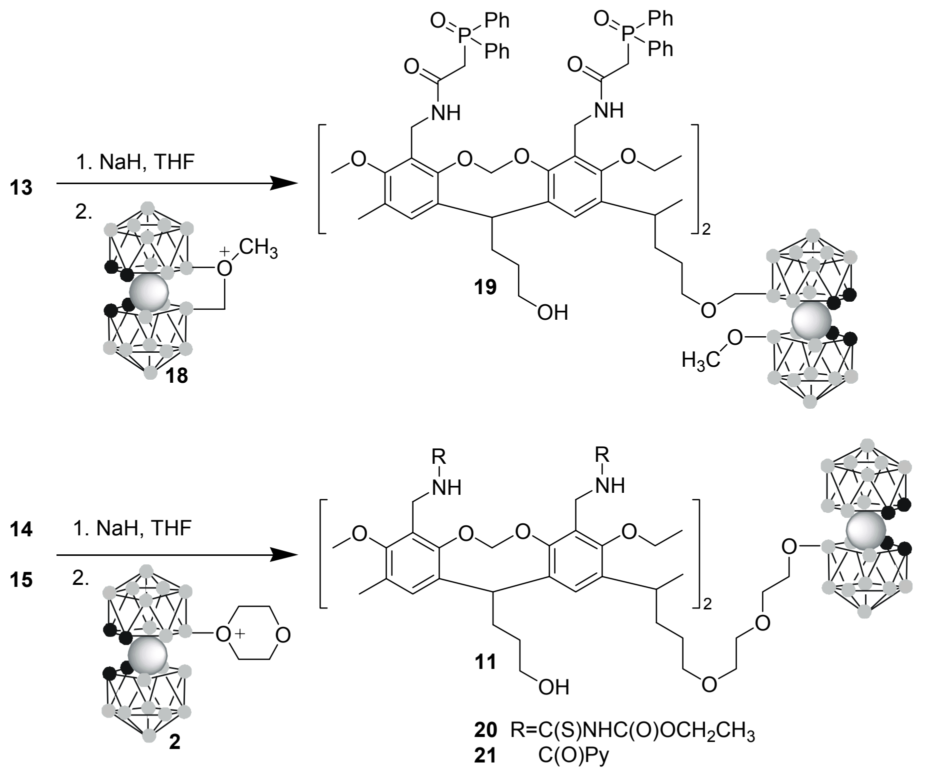
In previous chapters the attachment of ligating sites to cavitands has always been performed at the upper rim via an aminomethyl group. Therefore the synthesis of the additionally COSAN-functionalized cavitands starts from the known tetrakis(aminomethyl)-tetrakis(3-hydroxypropyl)cavitand **12** (Scheme 5.4).[15] The first attempt for the introduction of CMPO moieties was via reaction of **12** with chloroacetyl chloride. This reaction led to an unseparable mixture of products, probably due to the presence of two reactive sites, *viz*. the amino and hydroxy groups at the upper and lower rim, respectively. However, reaction of **12** with an activated CMPO-function, *p*-nitrophenyl (diphenylphosphoryl) acetate[16] (**16**), gave CMPO cavitand **13** in 54% yield. *N*-acylthiourea derivative **14** was obtained in 50% yield by reaction of **12** with ethoxycarbonyl isothiocyanate in methanol. Reaction of **12** with picolinic acid pentafluorophenyl ester[17] (**17**) in DMSO afforded picolinamide **15** in 35% yield.



Scheme 5.4.

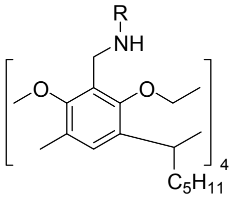
The formation of the tetrasubstituted cavitands **13**-**15** was clearly followed from the mass spectra and the symmetry in the ^{1}H NMR spectra. In addition to the specific signals of the ligating sites, the conservation of the singlet of the aromatic cavitand hydrogen and its downfield shift from 7.29 ppm in **12** to 7.36, 7.40, and 7.39 ppm for **13**, **14**, and **15**, respectively, is very characteristic.

The subsequent attachment of COSAN derivatives to cavitands **13**-**15** was performed by reaction with the COSAN dimethyl ether (yelloxide) derivative (**18**) and COSAN dioxane derivative **2** in the cases of **13** and **14**, **15**, respectively (Scheme 5.5) by the group of Dr. Grüner at the Institute of Inorganic Chemistry of the Academy of Sciences (Czech Republic).



Scheme 5.5.

As reference compounds for the extractions CMPO- (**22**), acylthiourea- (**23**), and picolinamide (**24**) cavitands were used (Chart 5.2). The synthesis of cavitands **22** and **23** has been described in Chapter 3. Cavitand **24** was easily prepared in 89% yield by reaction of tetrakis(aminomethyl)cavitand and picolinic acid pentafluorophenyl ester (**17**).[17]



22 R=$C(O)CH_2P(O)Ph_2$
23 $C(S)NHC(O)CH_2CH_3$
24 C(O)Py

Chart 5.2.

5.3 Extraction results

In order to study the efficiency of the different ionophores towards Eu^{3+} and Am^{3+}, liquid-liquid extractions were carried out.

Although compounds **6**, **9**, **10**, and **11** do not contain ligating sites, their extraction properties were tested for Eu^{3+}, as a representative of lanthanides and actinides, in order to study the possible influence of the cobalt bis(dicarbollide) (COSAN) moieties linked to the cavitand. As expected, compounds **9**, **10**, and **11** were ineffective in the extraction of Eu^{3+} ($D_{Eu}<0.01$ for 6.10^{-4}M **9** and 2.10^{-3}M **10** and **11** in toluene and 0.1M HNO_3). Surprisingly, compound **6**, with the COSAN groups linked at the phenolic positions, has a $D_{Eu}>20$ (conditions of the extraction: 4.10^{-4}M ligand in toluene and concentrations higher than 0.01M HNO_3).

Extractions of Eu^{3+} and Am^{3+} from 0.1M HNO_3 into nitrobenzene were performed with the COSAN-containing cavitands **19-21** and reference cavitands **22-24**. The results are summarized in Table 5.1.

Table 5.1. Distribution coefficients for the extraction of Eu^{3+} and Am^{3+} by COSAN-containing cavitands **19**-**21** and reference cavitands **22**-**24** (1M in nitrobenzene).[a]

Cation	COSAN-containing cavitands			Reference cavitands		
	19	**20**	**21**	**22**	**23**	**24**
Eu^{3+}	6.44	6.57	0.0082	2.18	$<10^{-3}$	0.002
Am^{3+}	7.60	6.12	0.011	3.01	0.001	0.006

a) Aqueous phase: 0.1M HNO_3.

COSAN-containing cavitands **19**-**21** present higher distribution coefficients than the reference cavitands **22**-**24**. The best extraction coefficients for Eu^{3+} and Am^{3+} were achieved with COSAN-containing CMPO cavitand **19**, although the distribution coefficients are only ~ 2.5 times higher than those of reference CMPO cavitand **22**. However, in the case of COSAN-containing *N*-acylthiourea cavitand **20**, the distribution coefficients are about 6000 times higher than those of reference *N*-acylthiourea cavitand **23**. The much smaller influence of the covalently bound COSAN on the distribution coefficients in the case of CMPO cavitand **19** compared with *N*-acylthiourea cavitand **20** may be attributed to the smaller spacer between the cavitand platform and the COSAN in **19**, preventing the COSAN from reaching the ligating sites. Comparison of **21** with **24**, having the same spacer, shows an increase in the distribution coefficients; however, it is not so pronounced as for the *N*-acylthioureas derivatives (**20** *vs* **23**). This may be due to the different chelating properties of the picolinamide *vs* *N*-acylthiourea groups.

Under the same conditions Eu^{3+} and Am^{3+} extractions were carried out with reference *N*-acylthiourea cavitand **23** in the presence of added Br_6-COSAN as a synergist, giving distribution coefficients of 0.002 and 0.014, respectively. Although there is a slight improvement compared with the extraction results of cavitand **23**, the superior effect of covalent linkage of COSAN (cavitand **20**; Table 5.1) is striking.

In the case of reference CMPO cavitand **22** there is a pronounced influence of the addition of Br_6-COSAN on the Eu^{3+} and Am^{3+} extraction, resulting in distribution coefficients of 57.6 and 229, respectively (2.18 and 3.01, respectively in the case of **22**; Table 5.1). A comparison with COSAN-containing CMPO cavitand **19** cannot be made, since in that case the COSAN is not really affecting the extraction properties (vide supra).

5.4 Conclusions

Liquid-liquid extraction experiments with COSAN-containing cavitands functionalized at the upper rim with CMPO- (**19**), *N*-acylthiourea- (**20**), or picolinamide (**21**) moieties for Eu^{3+} and Am^{3+} showed that they have higher distribution coefficients than the corresponding reference cavitands (**22**-**24**), although those of picolinamide containing cavitands **21** and **24** remain low. Remarkably, COSAN-containing *N*-acylthiourea cavitand **20** has about 6000 times better extraction efficiency than reference *N*-acylthiourea cavitand **23** and a synergistic mixture of hexabrominated bis(dicarbollide) anion (Br_6-COSAN) and **23**. The small difference between the distribution coefficients of COSAN-containing CMPO cavitand **19** and CMPO reference compound **22** indicates that the COSAN does not really participate in the extraction process, probably due to the short spacer between the COSAN and the cavitand platform in **19**. In general it can be concluded that covalent linkage of COSAN via a long and flexible spacer to the extractant has a positive effect on the extraction properties and is preferred over synergistic mixtures.

5.5 Experimental section

General

^1H and ^{13}C NMR spectra were recorded on a Varian Unity INOVA (300 MHz) and a Varian Unity 400 WB NMR spectrometer, respectively. Spectra were recorded in $CDCl_3$ or DMSO-d_6 at 295K. Residual solvent protons were used as an internal standard and chemical shifts are given in ppm relative to tetramethylsilane (TMS). Fast atom bombardment (FAB) mass spectra were measured on 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. Melting points (uncorrected) of all compounds were obtained on a Reichert melting point apparatus and on a Kofler stage.

Compounds **3**,[10] **4**,[11], and **5**[12] were prepared according to literature procedures.

Tetrakis(diphenyl-*N*-methylcarbamoylmethylphosphine oxide)-tetrakis(3-hydroxy-propyl)cavitand 13

A solution of tetrakis(aminomethyl)-tetrakis(3-hydroxypropyl)cavitand **12** (200 mg, 0.226 mmol) and CMPO active ester **16**[16] (517 mg, 1.356 mmol) in DMSO (50 mL) was heated at 100°C for 24 h. The solvent was removed in vacuo, and addition of EtOAc (10 mL) gave a precipitate. The precipitate was filtered off and stirred with a solution of 5% aq. $NaHCO_3$ (15 mL). The compound was extracted into CH_2Cl_2 (50 mL). Evaporation of the CH_2Cl_2 in vacuo gave **13** as a yellowish solid. Yield 122 mg (54%); mp 169-171°C; FAB-MS: *m/z* 1876.6 ($[M+Na]^+$, calcd 1876.8); ^1H NMR (DMSO-d_6) δ 8.03 (m, 4H, NH), 7.60-7.77 (m, 16H, P-phenyl), 7.45-7.52 (m, 24H, P-phenyl), 7.36 (s, 4H, ArH), 5.61 (d, 4H, *J*=7.7 Hz, OCH_2O), 4.57 (t, 4H, *J*= 8.4 Hz, ArCHAr), 4.45 (s, 8H, CH_2NH), 4.39 (d, 4H, *J*=7.7 Hz, OCH_2O), 4.13 (s, 8H, CH_2P) 3.65-3.40 (m, 8H, CH_2OH), 2.36-2.49 (m, 8H, CH_2), 1.22-1.48 (m, 8H, CH_2); ^{13}C NMR (DMSO-d_6) δ 153.7, 138.0, 132.4, 131.7, 130.9, 130.8, 128.9, 128.8, 123.0, 94.3, 62.3, 37.1, 31.3, 30.9, 30.8, 26.7. Anal. Calcd. for $C_{104}H_{100}N_4O_{20}\cdot 3/2CH_2Cl_2$: C, 63.98; H, 5.27; N, 2.84; Found: C, 64.18; H, 5.45; N, 2.68.

Tetrakis(ethoxycarbonylthioureidomethyl)-tetrakis(3-hydroxypropyl)cavitand 14

A solution of tetrakis(aminomethyl)-tetrakis(3-hydroxypropyl)cavitand **12** (150 mg, 0.17 mmol) and ethoxycarbonyl isothiocyanate (0.16 mL, 1.35 mmol) in dry methanol (50 mL) was refluxed for 72 h. The precipitate formed was filtered off and washed several times with a 2M solution of NaOH to afford a white residue. In order to remove any residual water, CH_2Cl_2 was added and the organic layer was dried over $MgSO_4$. Evaporation of CH_2Cl_2 gave **14** as a white solid. Yield 120 mg (50%); mp 252-254°C; FAB-MS: *m/z* 1409.8 ($[M+H]^+$, calcd 1409.8); ^1H NMR ($CDCl_3$) δ 9.8 (s, 4H, NH), 7.97 (s, 4H, NH), 7.40 (s, 4H, ArH), 6.07 (d, 4H, *J*=7.1 Hz, OCH_2O), 4.75-4.85 (m, 12H, CH_2N+ArCHAr), 4.43

(d, 4H, *J*=7.1 Hz, OCH_2O), 4.23 (q, 8H, *J*=7.1 Hz, CH_2O), 3.65-3.40 (m, 8H, CH_2OH), 2.38-2.51 (m, 16H, CH_2), 1.32 (t, 12H, *J*=7.1 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 178.8, 153.8, 152.5, 138.2, 121.9, 100.4, 62.9, 61.1, 40.3, 31.2, 27.0, 21.8, 14.2. Anal. Calcd. for $C_{64}H_{80}N_8O_{20}S_4\cdot5/2CH_2Cl_2$: C, 51.70; H, 5.49; N, 7.39; S, 8.46; Found: C, 51.29; H, 5.60; N, 7.21; S, 8.51.

Tetrakis(picolinamidomethyl)-tetrakis(3-hydroxypropyl)cavitand 15

A solution of tetrakis(aminomethyl)-tetrakis(3-hydroxypropyl)cavitand **12** (150 mg, 0.17 mmol) and picolinamide active ester **17**[17] (217 mg, 0.75 mmol) in dry DMSO (25 mL) was heated at 100°C for 3 days. The reaction mixture was evaporated to dryness and the residue taken up in a mixture of CH_2Cl_2 (50 mL) and H_2O (25 mL), whereupon the organic layer was washed with H_2O (100 mL) and evaporated to dryness. Trituration of the residue with Et_2O gave **15** as a white solid. Yield 75 mg (35%); mp 173-175°C; FAB-MS: *m/z* 1304.4 ($[M+H]^+$, calcd 1304.0); ^1H NMR ($CDCl_3$) δ 8.54 (d, 4H, *J*=4.4 Hz, ArH), 8.32 (t, 4H, *J*=6.2 Hz, NH), 8.13 (d, 4H, *J*=7.8 Hz, ArH), 7.83 (t, 4H, *J*=7.8 Hz, ArH), 7.42 (t, 4H, *J*=4.4 Hz, ArH), 7.39 (s, 4H, ArH), 6.13 (d, 4H, *J*=7.7 Hz, OCH_2O), 4.74 (t, 4H, *J*=8.0 Hz, ArCHAr), 4.41-4.58 (m, 12H, CH_2N, OCH_2O), 3.74-3.85 (m, 8H, CH_2OH), 2.40-2.53 (m, 16H, CH_2), 1.61 (bs, 4H, OH); ^{13}C NMR ($CDCl_3$) δ 163.9, 153.7, 149.7, 148.15, 138.0, 137.2, 126.2, 123.5, 122.3, 120.7, 62.6, 40.7, 37.3, 33.8, 31.2, 29.7, 26.8. Anal. Calcd. for $C_{72}H_{72}N_8O_{16}\cdot5/2CH_2Cl_2$: C, 58.96; H, 5.11; N, 7.38; Found: C, 59.09; H, 5.39; N, 7.35.

Tetrakis[(picolinamido)methyl]cavitand 24

A solution of tetrakis(aminomethyl)cavitand[18] (300 mg, 0.32 mmol) and picolinamide active ester (**17**)[17] (407 mg, 1.4 mmol) in THF (35 mL) was stirred at room temperature for 1 week. The reaction mixture was evaporated to dryness and redissolved in CH_2Cl_2 (70 mL). The solution was washed with H_2O (100 mL), and a sat. aq. sol. of $NaHCO_3$ (100 mL), and dried over $MgSO_4$. The resulting residue was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 100/0-90/10) to give **24** as a white solid. Yield 385 mg (89%); mp 116-118°C; FAB-MS: *m/z* 1353.5 ($[M+H]^+$, calcd 1353.7); ^1H NMR ($CDCl_3$) δ 8.44 (d, 4H, *J*=4.0 Hz, ArH), 8.21 (t, 4H, *J*=6.2 Hz, NH), 8.02 (d, 4H, *J*=7.8 Hz, ArH), 7.72 (t, 4H, *J*=7.8 Hz, ArH), 7.29-7.33 (m, 8H, ArH), 6.03 (d, 4H, *J*=7.3 Hz, OCH_2O), 4.74 (t, 4H, *J*= 8.0 Hz, ArCHAr), 4.35-4.40 (m, 12H, CH_2N, OCH_2O), 2.08-2.15 (m, 8H, CH_2), 1.20-1.33 (m, 24H, CH_2), 0.83 (t, 12H, *J*=7.0 Hz, CH_3); ^{13}C NMR δ ($CDCl_3$) δ 163.3, 153.3, 149.3, 147.6, 137.5, 136.6, 125.6, 123.2, 121.7, 119.3, 99.6, 33.3, 31.5, 29.7, 27.1, 22.1, 13.5; Anal. Calcd. for $C_{80}H_{88}N_8O_{12}$: C, 68.43; H, 6.36; N, 7.91; Found: C, 68.53; H, 6.35; N, 7.53.

Liquid-liquid extractions of Europium and Americium

All extraction experiments were performed in glass test tubes with polyethylene stoppers at laboratory temperature (23±1°C). The phase volume ratio was 1:1 (2 mL of each phase). The samples were shaken for 1 h (10 min was sufficient for reaching the extraction equilibrium) on a horizontal shaker. After shaking, the test tubes were centrifuged and 1 mL samples of each phase were taken for radioactivity measurements. The distribution of Eu^{3+} and Am^{3+} was investigated using carrier-free ^{152}Eu and ^{241}Am (radiochemical purity). The radioactivity of the samples was measured using a single-channel γ analyzer with a NaI (Tl) well detector.

5.6 References

[1] Plešek, J. *Chem. Rev.* **1992**, *92*, 269 and references cited therein.

[2] Plešek, J.; Heřmánek, S. *Collec. Czech. Chem. Commun.* **1995**, *60*, 1297.

[3] Teixidor, F.; Čásenký, B.; Dozol, J. F.; Heřmánek, S.; Mongeot, H.; Rais, J. *New Trends in the Separation of ^{137}Cs and ^{90}Sr and Transplutonium Elements from Radioactive HLW by Borane and Heteroborane Anions*. Final report EC-INCO-Copernicus, Contract CIPA-CT 93-1333, European Commission, Nuclear Science and Technology, Luxemburg, Office for Official Publications of the European Communities, **1998**.

[4] Romanovski, V. N. *Proceedings of the 5th International Information Exchange Meeting on Actinide and Fission Product Partitioning and Transmutation*, Mol, Belgium, Nov. 25-27, **1998**, p.77.

[5] (a)Plešek, J.; Grüner, B.; Heřmánek, S.; Báča, J.; Mareček, V.; Jänchenová, J.; Lhotský, A.; Holub, K.; Selucký, P.; Rais, J.; Císařová, I.; Cáslavský, J. *Polyhedron* **2002**, *21*, 975; (b) Sivaev, I. B.; Starikova, Z. A.; Sjöberg, S.; Bregadze, V. I. *J. Organomet. Chem.* **2002**, *649*, 1.

[6] (a)Viñas, C.; Gomez, S.; Beltran, J.; Teixidor, F.; Dozol, J. F.; Rouquette, H. *Inorg. Chem.* **1998**, *37*, 3640; (b) Viñas, C.; Beltran, J.; Gomez, S.; Barron, J.; Teixidor, F.; Dozol, J. F.; Rouquette, H.; Kivekäs, R.; Sillanpä, R. *J. Chem. Soc., Dalton Trans.* **1998**, 2849.

[7] Plešek, J.; Grüner, B.; Báča, J.; Císařová, I.; Dozol, J. F.; Rouquette, H.; Viñas, C.; Selucký, P.; Rais, J. *J. Organomet. Chem.* **2002**, *657*, 59.

[8] Grüner, B.; Plešek, J.; Báča, J.; Dozol, J. F.; Lamare, V.; Císařová, I.; Bělohradsky, M.; Cáslavský, J. *New J. Chem.* **2002**, *26*, 867.

[9] Grüner, B.; Plešek, J.; Císařová, I.; Báča, J.; Selucký, P.; Rais, J. *New J. Chem.* **2002**, *26*, 1519.

[10] Irwin, J. L.; Sherburn, M. S. *J. Org. Chem.* **2000**, *65*, 5846.

[11] Boerrigter H.; Lugtenberg, R. J. W.; Egberink, R. J. M.; Verboom, W.; Reinhoudt, D. N.; Spek, A. L. *Gazz. Chim. Ital.* **1997**, *127*, 709.

[12] Mezo, A. M.; Sherman, J. C. *J. Org. Chem.* **1998**, *93*, 6824.

[13] Plešek, J.; Heřmánek, S.; Franken, A.; Císařová, I.; Nachtigal, C. *Collec. Czech. Chem. Commun.* **1997**, *62*, 47.

[14] Grüner, B.; Mikulášek, L.; Báča, J.; Císařová, I.; Böhmer, V.; Danilla, C.; Reinoso García, M. M.; Verboom, W.; Reinhoudt, D. N.; Casnati, A. Manuscript in preparation.

[15] Middel, O.; Verboom, W.; Reinhoudt, D. N. *Eur. J. Org. Chem.* **2002**, 2587.

[16] 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.

[17] Christensen, J. B. *Molecules* **2001**, *6*, 47.

[18] Boerrigter, H.; Verboom, W.; Reinhoudt, D. N. *J. Org. Chem.* **1997**, *62*, 7148.

Chapter 6

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

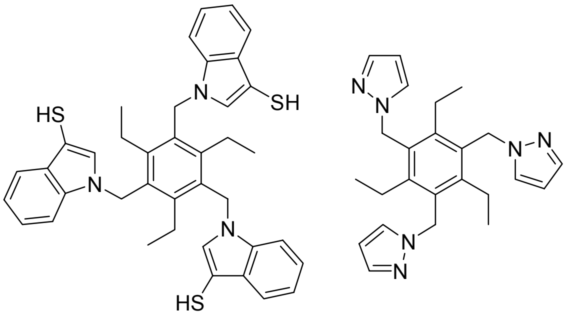
The synthesis and binding properties towards different cations of a series of tripodal ligands functionalized with N-*acyl(thio)urea- and picolin(thio)amide- moieties are described. For the extraction of* Am^{3+} *and* Eu^{3+} *the compounds are not efficient; however,* N-*acylurea derivative* ***17*** *exhibits a significant selectivity for* Am^{3+} *over* Eu^{3+} ($S_{Am/Eu} \sim 30$)*. Upon addition of the synergistic hexabrominated cobalt bis(dicarbollide) anion* (Br_6-*COSAN) the distribution coefficients for* Am^{3+} *and* Eu^{3+} *increase up to 1000-fold for picolinamide derivative* ***18****. 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* ***18*** *is a very selective and strong ionophore for* Hg^{2+} *and that* N-*acylurea* ***16*** *is a very good ionophore for* Ag^{+}*. Potentiometric studies with electrodes reveal that* N-*acyl(thio)urea and picolin(thio)amide derivatives (****14****-****20****) have a considerable enhancement of the selectivity towards* Ag^{+} *or* Pb^{2+} *over* Na^{+} *ions.*

6.1 Introduction

The ability of calix[n]arene-based (macrocyclic) ligands to bind neutral and ionic guest species, depend on the attached pendant functionalities.[1] In previous Chapters it was shown that cavitands with four ligating carbamoylmethylphosphonate (CMP) and –phosphine oxide (CMPO) groups are good chelating agents for actinides and lanthanides. More flexible ligating sites gave rise to better extraction results.

For actinide or lanthanide complexation only three pendant arms are necessary. For example, a 3:1 stoichiometry (CMPO to metal) is needed to extract americium cations from the acidic aqueous phase into the organic phase during the TRUEX process.[2] Unfortunately, macrocycles with only three pendant arms are difficult to prepare. Only a few examples are known using the C_3-symmetrical cyclotriveratrylene (CTV) as a scaffold.[3] However, in order to avoid extensive synthetic effort, it would be favorable to exploit relatively simple platforms with a C_3-symmetry.

Nowaday, there is a growing interest in tripodal ionophores with C_3-symmetry, which are used for the analysis of metal ions and have different biological applications.[4,5,6,]



1 2

Chart 6.1.

1,3,5-Substituted-2,4,6-triethylbenzenes (Chart 6.1) are used as C_3-symmetrical molecular platforms, due to their characteristic conformation; the ethyl groups at the 2-, 4-, and 6- positions ensure that all the ligating groups are pointing in the same direction.[7] This scaffold has been used in receptors for cations (Fe^{3+},[8] Cu^+,[9] NH_4^+,[10] etc) and anions.[11] However, no flexibility in the arms has been introduced so far.

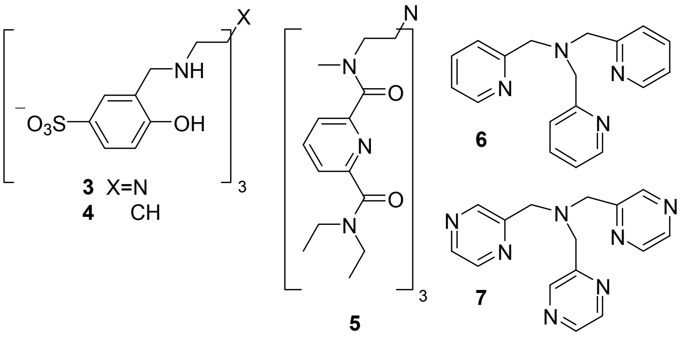
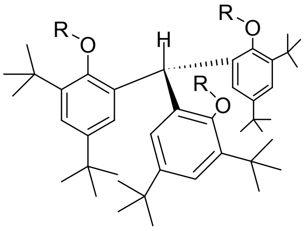


Chart 6.2.

Tripodal ionophores composed of three chelating units connected to a nitrogen (tren-derivatives) (**3** and **5**) or carbon atom (**4**) (Chart 6.2) are well known to have a high affinity for lanthanides,[12,13,14] which makes them useful luminescent probes in medicine and biology.[15] The connection of three 2-pyridylmethyl **6** or 2-pyrazinyl **7** moieties to a nitrogen atom leads to ionophores that extract selectively actinides in the presence of lanthanides (Chart 6.2).[16]

The triphenoxymethanes comprise a class of compounds with C_3-symmetry that are more rigid.[17] Attachment of three CMPO moieties gave an ionophore (**8**) with enhanced selectivity for Th^{4+} over lanthanides.[18] Shanzer and coworkers used tripodal structures with flexible arms (**9**), based on trimethylolpropane, for the complexation of Ca^{2+}.[19] The commercially available Na^+ ionophore **10** is based on the same skeleton (Chart 6.3).[20]



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

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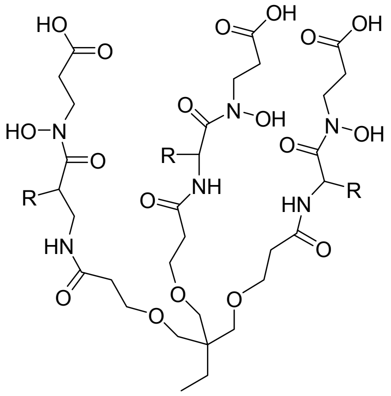

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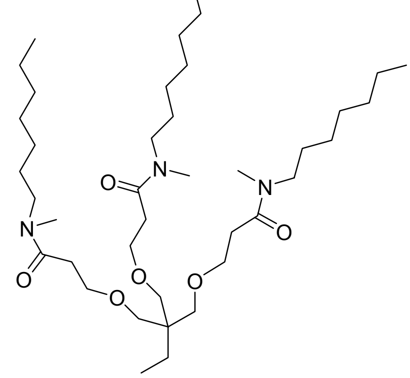

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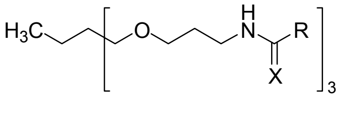
Chart 6.3.

In this Chapter the synthesis, extraction, and sensing behavior of trimethylolpropane-based tripodal ionophores with *N*-acyl(thio)urea and picolin(thio)amide ligating sites will be discussed (Chart 6.4). An extensive study of this platform functionalized with CMP(O) moieties is described in Chapter 7.

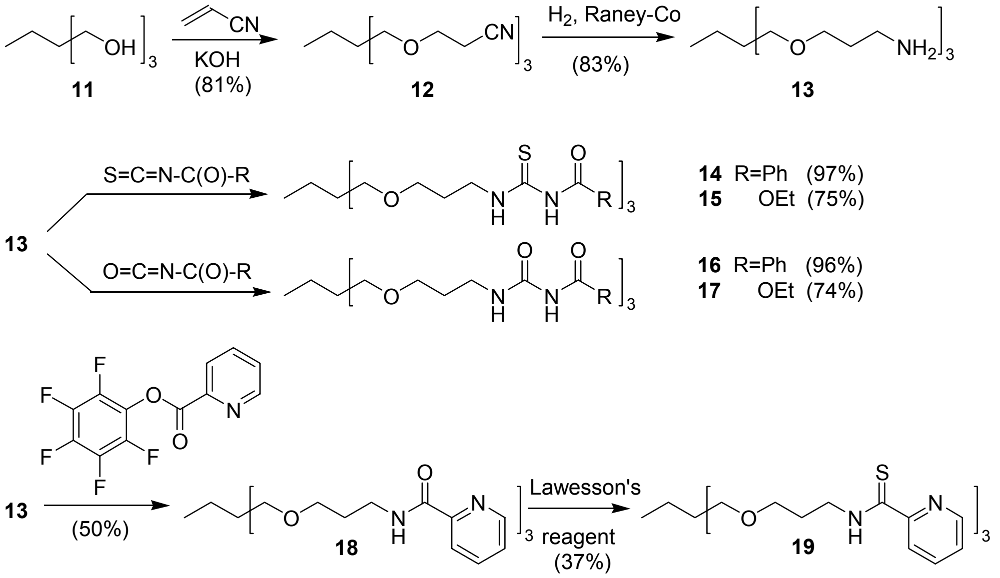


	X	R
14	X=S,	R=NHC(O)Ph
15	S	NHC(O)OEt
16	O	NHC(O)Ph
17	O	NHC(O)OEt
18	O	Py
19	S	Py

Chart 6.4. Structure of ionophores used in this Chapter.

6.2 Synthesis

The synthesis of the C_3-symmetric tripodal ligands **14-19** is summarized in Scheme 6.1. The known reaction of trimethylolpropane **11** with acrylonitrile, using KOH as a base, afforded the Michael adduct **12** as a yellow oil in 81% yield.[6,19] Catalytic hydrogenation of **12** with Raney-Co gave 1,1,1-tris[(aminopropoxy)-methyl]propane **13** 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.

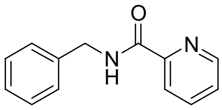


Scheme 6.1.

Subsequent reaction of **13** with the appropriate iso(thio)cyanates in acetonitrile gave compounds **14**, **15**, **16**, and **17** in 97%, 75%, 96%, and 74% yield, respectively. In all cases the introduction of the acyl(thio)urea groups induced a downfield shift in the ^1H NMR spectra for the methylene protons next to the chelating group, from 2.80 in **13** to 3.79 and 3.78 ppm for the acylthioureas **14** and **15**, and to 3.41-3.51 and 3.40 ppm for the acylureas **16** and **17**, respectively.

Picolinamido derivative **18** was obtained in 50% yield by reaction of **13** with pentafluoro picolinamide ester in dry THF. The downfield shift in the ^{1}H NMR spectrum of the methylene protons adjacent to the picolinamide from 2.80 in **13** to 3.60 ppm confirmed its formation. Subsequent reaction of **18** with Lawesson's reagent in refluxing toluene afforded picolinthioamide derivative **19** in 37% yield.

Model compound **20** (Chart 6.5) was synthesized following a literature procedure.[21]



20

Chart 6.5.

6.3 Liquid-liquid Extractions

6.3.1 Extraction of Americium and Europium

In order to study whether compounds **14-18** 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 extraction method was similar to the procedure described in Chapter 3.

The results with compounds **14-18** are summarized in Table 6.1. The extraction data are expressed as distribution coefficients which are the ratios of the metal concentrations in the organic phase and in the aqueous phase (see Chapter 3, experimental section).

Table 6.1. Distribution coefficients for the extraction of Eu^{3+} and Am^{3+} by tripodal derivatives **14-18**.[a]

Ionophore	Cation	HNO$_3$ concentration					
		0.001M	0.01M	0.1M	1M	2M	3M
14	Eu^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
	Am^{3+}	0.001	0.001	0.001	0.002	0.004	0.005
15	Eu^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
	Am^{3+}	n.d.[b]	n.d.[b]	n.d.[b]	0.003	0.004	0.004
16	Eu^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
	Am^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	0.001	0.008	0.004
17	Eu^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
	Am^{3+}	0.001	0.001	0.003	0.016	0.029	0.030
18	Eu^{3+}	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$	$<10^{-3}$
	Am^{3+}	0.004	0.001	0.001	0.001	0.002	0.003

a) Aqueous phase: 152-Eu; 241-Am / [HNO$_3$] variable (~1500 kBq/L)/(Sp Gamma D3/0.5 mL).
Organic phase: 10^{-3}M ligand in *o*-nitrophenyl hexyl ether (NPHE).
b) Not determined.

Table 6.1 shows that all compounds have low distribution coefficients, they are neither effective nor selective. However, *N*-acylurea derivative **17** exhibits higher distribution coefficients for Am^{3+} than the *N*-acylurea tetrafunctionalized cavitand reported in Chapter 3, especially at high nitric acid concentrations (D=0.03 *vs* 10^{-3} at 2-3M nitric acid). The extraction behavior of *N*-acylurea **17**, having two hard donor atoms, is striking. Ionophore **17** is the most effective, in comparison with the other compounds studied, but the most important feature is its high selectivity at nitric acid concentrations higher than 1M, reaching separation factors of ~ 30. On the other hand the distribution coefficients are low. The results obtained with picolinamide derivative **18** were disappointing, showing no affinity and no selectivity for Am^{3+} and Eu^{3+}. Picolinamide is a soft donor extractant, which in general shows a selectivity towards actinides over lanthanides.[22,23]

Table 6.2. Distribution coefficients for the extraction of Eu^{3+} and Am^{3+} by tripodal derivatives **14-18** in the presence of Br_6-COSAN as a synergist.[a]

Ionophore	Cation	HNO_3 concentration					
		0.001M	0.01M	0.1M	1M	2M	4M
14	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
15	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
16	Eu^{3+}	109.00	0.492	0.017	0.005	0.002	0.119
	Am^{3+}	84.20	0.794	0.033	0.009	0.006	0.009
17	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
18	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 (~1500 kBq/L)/(Sp Gamma D3/0.5 mL).
Organic phase: 10^{-3}M ligand + 3.10^{-3}M Br_6-COSAN in NPHE.

Upon the addition of Br_6-COSAN (see Chapter 3) as a synergist a considerable enhancement of the extraction properties is achieved (Table 6.2). In all cases the distribution coefficients increase, most pronouncably at 0.001M HNO_3. The high distribution coefficients (>1000 at 0.01M and 0.001M HNO_3) obtained with picolinamide derivative **18** are remarkable. For the *N*-acyl(thio)urea derivatives **14**-**17** the distribution coefficients range between 0.5 and 770 at ≤0.01M HNO_3. In case of the corresponding cavitands, distribution coefficients between 0.1 and >100 were obtained under the same extraction conditions (see Chapter 3).

6.3.2 Picrate extractions

In order to study the extraction behavior of compounds **14**, **15**, **16**, and **18** 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 extractions experiments were performed. The results, expressed as a percentage of cation extracted (%E), are shown in Table 6.3 and represented graphically in Figure 6.1. Significant differences in complexation can be observed depending on the chelating groups (*N*-acyl(thio)ureas and picolinamide). Picolinamide derivative **18** shows a very low extraction affinity towards most of the cations examined (%E <20, except for Hg^{2+}).

Table 6.3. Percentage of cation extracted (%E) by tripodal derivatives **14**, **15**, **16**, and **18**.[a]

Ionophore	Na^+	K^+	Ag^+	Ca^{2+}	Cd^{2+}	Hg^{2+}	Pb^{2+}	Cu^{2+}	Fe^{3+}	Eu^{3+}
14	13	26	69	22	18	41	21	33	24	22
15	18	32	84	25	25	56	42	43	29	24
16	20	34	70	27	29	45	24	42	25	21
18	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.

From Table 6.3 it is clear that thiourea **15** is a better transfer agent than **14** and **16**; it has higher extraction values for most of the cations studied. All the *N*-acyl(thio)urea derivatives show a high preference for Ag^+, especially thiourea **15**, the extraction value (84%) of which is comparable to those obtained with *N*-acylthiourea-tetrafunctionalized cavitands (Chapter 4) and sulphur-containing calix[4]arene-based ionophores.[24] In the case of the calixarenes 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 (**14** *vs* **15**) than between thiourea **14** and urea **16** (Figure 6.1). Ionophore **15** with –C(O)OEt moieties is a more effective extractant than **14** containing –C(O)Ph groups. This can be explained by the fact that –C(O)OEt moieties interact more strongly than –C(O)Ph groups with hard and soft Lewis acids.[25] In addition, the –C(O)OEt substituents are smaller and more flexible than the –C(O)Ph moieties.

Picolinamide derivative **18** is a less efficient extractant than the *N*-acyl(thio)urea derivatives. Although picolinamide moieties are known to form strong complexes with Cu^{2+},[26] the extraction efficiency of **18** for Cu^{2+} is low (16%). On the other hand, **18** has a remarkably high affinity for Hg^{2+} compared to Ag^{+} (44% *vs* 5%). Probably, the observed selectivity originates from the presence of both a hard (C=O group) and a soft (pyridine) donor atom and the harder character of Hg^{2+} in comparison with Ag^{+}.

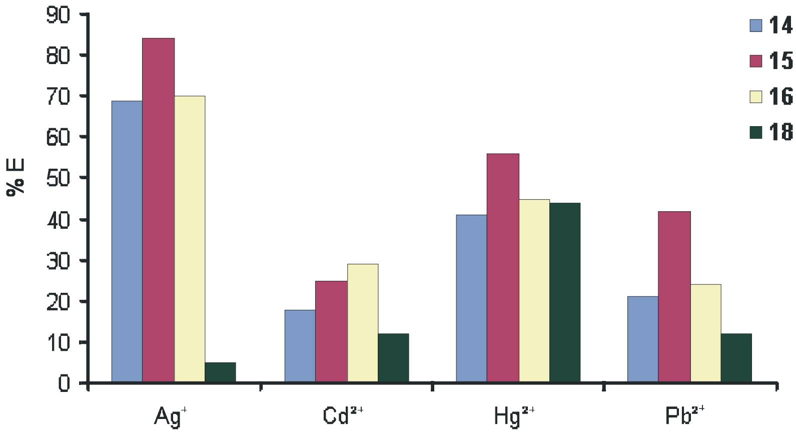


Figure 6.1. Extraction percentage (%E) of silver and heavy metals into CH_2Cl_2 at 25°C by tripodal derivatives **14**, **15**, **16** and **18**.

6.4 Potentiometric studies

The selectivities of compounds **14-20**, in terms of the potentiometric selectivity coefficients ($K_{i,j}^{pot}$), were evaluated using polymeric membrane-based ion-selective electrodes (ISEs) (see also Chapter 4). The polymeric membrane was composed of compounds **14-20** as the ionophore (1 wt%), poly(vinyl chloride) (PVC; 33 wt%) as membrane matrix, *o*-nitrophenyl octyl ether (*o*-NPOE; 66 wt%) as the plasticizer, and 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.

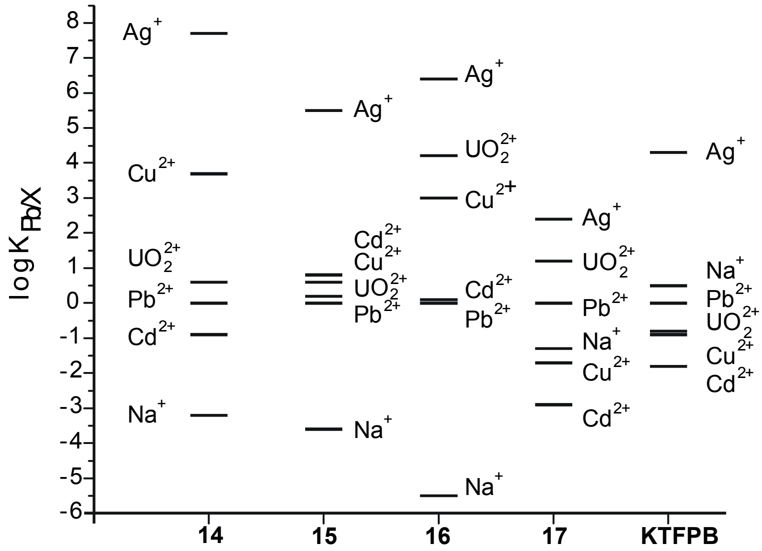


Figure 6.2. Selectivity coefficients for electrodes prepared with PVC/*o*-NPOE (1:2 by weight) membranes containing *N*-acyl(thio)urea derivatives **14**, **15**, **16**, and **17** and lipophilic sites (KTFPB), as well as membranes with ion-exchanger only, with Pb^{2+} as the primary cation.

To obtain unbiased $K_{i,j}^{pot}$ values, the calibration plots for various cations were collected starting from the most discriminating ones.[27] The preliminary selectivity order for each ionophore was established after 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 flattening (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 ($\log K_{i,j}^{pot}$) are presented in Figures 6.2 and 6.3. Comparison of the results obtained for membranes containing *N*-acyl(thio)ureas (**14**-**17**) and picolin(thio)amide derivatives (**18**-**20**) with those of membranes containing only ion-exchanger (KTFPB), revealed that ionophores **14**-**20** induce considerable changes in the electrode selectivity for Pb^{2+} over Na^+. The behavior of *N*-acylthioureas and *N*-acylureas in the membrane is more or less the same except for UO_2^{2+} cations. *N*-acylurea derivative **16** has a much better selectivity towards the harder UO_2^{2+} than towards Pb^{2+}.

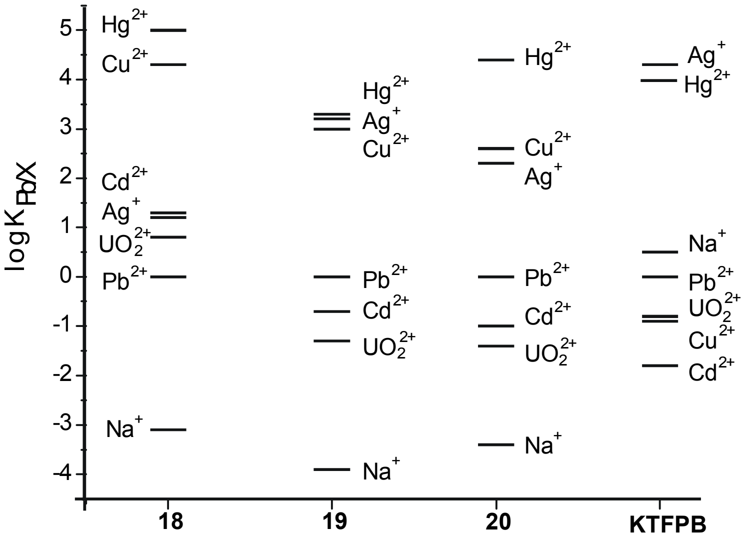


Figure 6.3. Selectivity coefficients for electrodes prepared with PVC/*o*-NPOE (1:2 by weight) membranes containing picolin(thio)urea derivatives **18**, **19**, and **20** and lipophilic sites (KTFPB) as well as membranes with ion-exchanger only, with Pb^{2+} as the primary cation.

N-acylthiourea derivatives **14** and **15** have a soft ligating C=S group, therefore the electrodes with membranes based on these ionophores showed an enhanced selectivity towards Ag^+, compared to membranes with only cation-exchanger.

Electrodes with picolin(thio)amide derivatives **18**-**20** exhibited an enhanced selectivity towards Hg^{2+}. The largest value of log $K^{pot}_{Pb,Hg}$ was determined for picolinamide **18**. The values of **18** and **19** for $K^{pot}_{Pb,Hg}$ are only roughly estimated, because during the 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 **18** (in concordance with the high extraction data found by the picrate method; vide supra) and changes in the ionophore structure (membranes become darker) in the case of picolinthioamide **19**. All membranes that contain *N*-acylthioureas or picolin(thio)amides provided an increased selectivity towards Cu^{2+} in comparison with the membranes with *N*-acylureas and without ionophore. The log $K^{pot}_{Pb,Cu}$ values for picolin(thio)amides **18** and **19** are again roughly estimated. In the case of ionophore **18** a change of the oxidation state (from Cu^{2+} to Cu^{+}) is possible. For picolinthioamide **19** a change in the color of the membranes was observed, indicating changes in the ionophore structure. A similar phenomenon, as observed for **18** and **19** towards Hg^{2+} and Cu^{2+} cations, has been reported before for azothiacrown ethers.[28]

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.[29] However, the main factor that is primarily responsible for the selectivity of ion-ionophore interactions can be expressed by the relative stability constants of complexes formed by an ionophore with primary and interfering ions within the membrane phase.

Table 6.4. Formal complex formation constants, log β_{ML}, obtained with ionophores **14**-**20** in PVC/*o*-NPOE (1:2) membranes, using the segmented sandwich method.

Ionophore / Cation	*N*-acyl(thio)urea				Picolin(thio)amide		
	14	**15**	**16**	**17**	**18**	**19**	**20**
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+}	10.6	>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	4.8	16.3	8.1
UO_2^{2+}	14.9	15.4	15.4	11.0	13.6	12.4	8.3
Hg^{2+}	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]	>10.4	>10.6	8.4

a) Not determined.

The complex formation constants were determined by means of the segmented sandwich method.[30] The values of the complex formation constants with a range of cations are collected in Table 6.4. *N*-acylthiourea derivatives **14** and **15** have the highest formation constant for Cd^{2+}, whereas *N*-acylurea derivatives **16** and **17** form strong complexes with Cu^{2+}; towards the other cations studied they present the same profile.

The values of picolin(thio)amides **18** and **19** for Cu^{2+} and Hg^{2+} have to be treated as an approximation due to the non-linear response of the membranes with **18** and **19** to the logarithm of the Cu^{2+} and Hg^{2+} activity in sample solutions. Unfortunately, this is a limitation of the method.

From a comparison of the data of picolinamide model compound **20** with those of tripodal picolinamide **18**, it is clear that the attachment of three picolinamide moieties to the tripodal platform led to significant differences of their selectivity coefficients (Table 6.3) 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.

6.5 Conclusions

A series of simple C_3-symmetrical trimethylolpropane-based ionophores with *N*-acyl(thio)urea (**14**-**17**) and picolin(thio)amide (**18** and **19**) ligating sites were prepared. *N*-acylurea derivative **17** 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 **18** a distribution coefficient of >1000 was obtained.

N-acyl(thio)ureas **14**-**17** are good ionophores for the extraction and detection of Ag^+, especially compound **15**, which has the highest affinity (84%); the extraction profile is comparable to those obtained with preorganized ligands (cavitands, calixarenes). Picolinamide derivative **18** 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 **16** 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 **18** and **19** form complexes with Cu^{2+} and Hg^{2+} which are so strong that they cannot be used as ionophores on ion selective electrodes, although they are very useful ionophores for liquid-liquid extractions.

6.6 Experimental Section

General

^1H and ^{13}C NMR spectra were recorded on 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 an internal standard and chemical shifts are given in ppm relative to tetramethylsilane (TMS). Fast atom bombardment (FAB) mass spectra were measured on 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 **12** was prepared following a literature procedure.[6]

Extractions of Am^{3+} and Eu^{3+} were performed as described in Chapter 3. Picrate extractions and potentiometric measurements were performed as described in Chapter 4.

1,1,1-Tris[(aminopropoxy)methyl]propane 13

A solution of tris(cyanoethyl) tripodand **12** (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 **13** as a yellow oil. Yield 867 mg (83%). FAB-MS: *m/z* 306.2 ($[M+H]^+$, calcd 306.0); ^{1}H NMR δ 3.42 (t, 6H, *J*=6.2 Hz, OCH_2), 3.23 (s, 6H, CH_2O), 2.80 (t, 6H, *J*=6.6 Hz, CH_2NH_2), 1.63-1.70 (m, 6H, CH_2), 1.20 (q, 2H, *J*=7.7 Hz, CH_2), 0.86 (t, 3H, *J*=7.7 Hz, CH_3); ^{13}C NMR δ 71.9, 69.6, 42.7, 39.3, 23.9, 7.0.

General Procedure for the Preparation of (Thio)urea Tripodal Compounds 14-17

A solution of 1,1,1-tris[(aminopropoxy)methyl]propane **13** 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 **14-17**.

Benzoyl thiourea tripodand 14 was prepared from **13** (1.10 g, 3.60 mmol) and benzoyl isothiocyanate (1.46 mL, 10.8 mmol) as a yellow oil. Yield 2.76 g (97%); FAB-MS: *m/z* 794.1 ($[M+H]^+$, calcd 794.3); ^{1}H NMR δ 9.02 (s, 3H, CSNHCO), 7.54-7.89 (m, 6H, ArH), 7.00-7.50 (m, 9H, ArH), 6.80-6.85 (m, 3H, CH_2NHCO), 3.79 (q, 6H, *J*=6.6 Hz, CH_2NH), 3.42-3.60 (m, 6H, OCH_2), 3.25 (s, 6H, CH_2O), 1.82-1.90 (m, 6H, CH_2), 1.45 (q, 2H, *J*=7.5 Hz, CH_2), 0.86 (t, 3H, *J*=7.5 Hz, CH_3); ^{13}C NMR δ 179.0, 167.0, 133.0, 131.0, 128.5, 127.0, 71.0, 68.0, 43.0, 38.5, 28.5, 27.5, 7.0.

Ethoxycarbonyl thiourea tripodand 15 was prepared from **13** (1.05 g, 3.44 mmol) and ethoxycarbonyl isothiocyanate (1.2 mL, 10.6 mmol) as a yellow oil. Yield 1.80 g (75%);

FAB-MS: *m/z* 698.2 ($[M+H]^+$, calcd 698.3); ^1H NMR δ 9.70 (s, 3H, NH), 8.18 (s, 3H, NH), 4.20 (q, 6H, *J*=7.1 Hz, OCH_2), 3.78 (q, 6H, *J*=6.6 Hz, CH_2NH), 3.42 (t, 6H, *J*=5.8 Hz, OCH_2), 3.30 (s, 6H, CCH_2O), 1.87-1.95 (m, 6H, CH_2), 1.42 (q, 2H, *J*=7.3 Hz, CH_2), 1.29 (t, 9H, *J*=7.1 Hz, CH_3), 0.81 (t, 3H, *J*=7.3 Hz, CH_3); ^{13}C NMR δ 178.5, 152.0, 71.0, 68.5, 62.0, 43.0, 42.0, 24.0, 22.5, 14.0, 7.0.

Benzoyl urea tripodand 16 was prepared from **13** (1.19 g, 3.90 mmol) and benzoyl thiocyanate (1.5 mL, 11.9 mmol) as a yellow oil. Yield 2.79 g (96%); FAB-MS: *m/z* 747.4 ($[M+H]^+$, calcd 747.6); ^1H NMR δ 9.00 (s, 3H, NH), 7.51-7.57 (m, 6H, ArH), 7.44-7.47 (m, 9H, ArH), 3.41-3.51 (m, 12H, OCH_2+CH_2NH), 3.48 (s, 6H, CH_2O), 1.81-1.91 (m, 6H, CH_2), 1.26 (q, 2H, *J*=7.3 Hz, CH_2). 0.81 (t, 3H, *J*=7.3 Hz, CH_3); ^{13}C NMR δ 179.0, 166.0, 128.5, 128.0, 124.5, 124.0, 71.0, 68.0, 43.5, 38.0, 28.0, 22.5, 7.5.

Ethoxycarbonyl urea tripodand 17 was prepared from **13** (850 mg, 2.78 mmol) and ethoxycarbonyl isocyanate (0.87 mL, 8.35 mmol) as a yellow oil. Yield 1.33 g (74%); FAB-MS: *m/z* 650.2 ($[M+H]^+$, calcd 650.3); ^1H NMR δ 7.82 (s, 3H, NH), 7.35 (s, 3H, NH), 4.44 (q, 6H, *J*=7.1 Hz, OCH_2), 3.45 (t, 6H, *J*=5.8 Hz, OCH_2), 3.40 (q, 6H, *J*=6.6 Hz, CH_2NH), 3.25 (s, 6H, CH_2O), 1.75-1.81 (m, 6H, CH_2), 1.38 (q, 2H, *J*=7.1 Hz, CH_2), 1.25 (t, 9H, *J*=7.1 Hz, CH_3), 0.81 (t, 3H, *J*=7.1 Hz, CH_3); ^{13}C NMR δ 153.0, 128.0, 71.0, 68.0, 62.0, 42.5, 37.0, 29.0, 22.5, 13.5, 7.5.

Tris(picolinamide) tripodand 18

A solution of 1,1,1-tris[(aminopropoxy)methyl]propane **13** (1.32 g, 4.32 mmol) and pentafluoro picolinamide ester[31] (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 bicarbonate (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 **18** as a brownish oil. Yield 1.34 g (50%); FAB-MS: *m/z* 621.4 ($[M+H]^+$, calcd 621.3); ^1H NMR δ 8.52 (d, 3H, *J*=4.7 Hz, ArH), 8.36-8.38 (m, 3H, NH), 8.20 (d, 3H, *J*=7.7 Hz, ArH), 7.85 (t, 3H, *J*=7.7 Hz, ArH), 7.40 (t, 3H, *J*=4.7 Hz, ArH), 3.60 (q, 6H, *J*=5.8 Hz, CH_2NH), 3.52 (t, 6H, *J*=5.8 Hz, OCH_2), 3.47 (s, 6H, CH_2O), 1.88 (q, 6H, *J*=5.8 Hz, CH_2), 1.62 (q, 2H, *J*=7.7 Hz, CH_2), 0.89 (t, 3H, *J*=7.7 Hz, CH_3); ^{13}C NMR δ 162.0, 145.0, 136.5, 125.5, 122.0, 71.0, 69.5, 42.5, 37.0, 28.0, 22.0, 7.5.

Tris(picolinthioamide) tripodand 19

A mixture of **18** (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 **19** as a brownish oil. Yield 50 mg (37%); FAB-MS: *m/z* 669.0 ($[M+H]^+$, calcd 669.5); ^{1}H NMR δ 8.42 (d, 3H, *J*=4.7 Hz, ArH), 8.28-8.30 (m, 3H, NH), 8.20 (d, 3H, *J*=7.7 Hz, ArH), 7.85 (t, 3H, *J*=7.7 Hz, ArH), 7.40 (t, 3H, *J*=4.7 Hz, ArH), 3.49 (q, 6H, *J*=5.8 Hz, CH_2NH), 3.43 (t, 6H, *J*=5.8 Hz, OCH_2), 3.38 (s, 6H, CH_2O), 1.79 (q, 6H, *J*=5.8 Hz, CH_2), 1.62 (q, 2H, *J*=7.7 Hz, CH_2), 0.79 (t, 3H, *J*=7.7 Hz, CH_3); ^{13}C NMR δ 164.2, 150.1, 147.9, 137.1, 125.9, 122.1, 71.6, 70.2, 43.2, 37.9, 28.0, 22.8, 7.7.

6.7 References

[1] *Calixarenes 2001*, Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic Publishers, Dordrecht, **2001**.

[2] (a) Horwitz, E. P.; Martin, K. A.; Diamond, H.; Kaplan, L. *Solvent Extr. Ion Exch.* **1986**, *4*, 449; (b) Horwitz, E. P.; Diamond, H.; Martin, K. A.; Chiarizia, R. *Solvent Extr. Ion Exch.* **1987**, *5*, 419.

[3] Veriot, G.; Dutasta, J. P.; Matuozenko, G.; Collet, A. *Tetrahedron* **1995**, *51*, 389.

[4] Goodall, M.; Kelly, P. M.; Peter, D. *J. Chem. Soc., Perkin Trans. 2* **1997**, 59.

[5] Gelinsky, M.; Vogler, R.; Vahrenkamp, H. *Inorg. Chem.* **2002**, *41*, 2560.

[6] Meijler, M. M.; Arad-Yellin, R.; Cabantchik, Z. I.; Shanzer, A. *J. Am. Chem. Soc.* **2002**, *124*, 12666.

[7] (a) Kilway, K. V.; Siegel, J. S. *J. Am. Chem. Soc.* **1991**, *113*, 2332; (b) Kilway, K. V.; Siegel, J. S. *Tetrahedron*, **2001**, *57*, 3615.

[8] (a) Stack, T. D. P.; Hou, Z.; Raymond, K. N. *J. Am. Chem. Soc.* **1993**, *115*, 6466; (b) Hou, Z.; Stack, T. D. P.; Sunderland, C. J.; Raymond, K. N. *Inorg. Chim. Acta* **1997**, *263*, 341; (c) Hay, B. P.; Dixon, D. A.; Vargas, A.; Garza, J.; Raymond, K. N. *Inorg. Chem.* **2001**, *40*, 3922.

[9] Walsdorff, C.; Park, S.; Kim, J.; Heo, J.; Park, K. M.; Oh, J.; Kim, K. *J. Chem. Soc., Dalton Trans.* **1999**, 923.

[10] Kim, S. G.; Ahn, K. H. *Chem. Eur. J.* **2000**, *6*, 3399.

[11] Hennrich, G.; Anslyn, E. V. *Chem. Eur. J.* **2002**, *8*, 2219.

[12] Caravan, P.; Hedlund, T.; Liu, S.; Sjöberg, S.; Orvig, C. *J. Am. Chem. Soc.* **1995**, *117*, 11230.

[13] Lowe, M. P.; Caravan, P.; Rettig, S. J.; Orvig, C. *Inorg. Chem.* **1998**, *37*, 1637.

[14] Renaud, F.; Piguet, C.; Bernardinelli, G.; Bünzli, J. C. G.; Hopfgartner, G. *J. Am. Chem. Soc.* **1999**, *121*, 9326.

[15] Bünzli, J. C. G. *Lanthanide Probes in Life, Chemical and Earth Sciences*; Elsevier: Amsterdam, The Netherlands, **1989**.

[16] (a) Wietzke, R.; Mazzanti, M.; Latour, J. M.; Pecaut, J.; Cordier, P. Y.; Madic, C. *Inorg. Chem.* **1998**, *37*, 6690; (b) Mazzanti, R.; Wietzke, R.; Pecaut, J.; Latour, J. M.; Maldivi, P.; Remy, M. *Inorg. Chem.* **2002**, *41*, 2389.

[17] (a) Casiraghi, G.; Casnati, G.; Cornia, M.; D'Azeglio, V. *Tetrahedron Lett.* **1973**, 679; (b) Casiraghi, G.; Casnati, G.; Cornia, M.; Pochini, A. *Gazz. Chim. Ital.* **1978**, *108*, 79.

[18] Peters, M. W.; Werner, E. J.; Scott, M. J. *Inorg. Chem.* **2002**, *41*, 1707.

[19] Dayan, I.; Libman, J.; Shanzer, A.; Felder, C. E.; Lifson, S. *J. Am. Chem. Soc.* **1991**, *113*, 3431.

[20] (a) Steiner, R. A.; Oehme, M.; Ammann, D.; Simon, W. *Anal. Chem.* **1979**, *51*, 351; (b) Simon, W.; Carafoli, E. *Meth. Enzymol.* **1979**, *56*, 439.

[21] Gou, Z.; Dowdy, E. D.; Li, W. S.; Polniaszek, R.; Delaney, E. *Tetrahedron Lett.* **2001**, *42*, 1843.

[22] Kwon, S. G.; Lee, E. H.; Yoo, J. H.; Park, H. S.; Kim, J. S. *J. Kor. Nucl. Soc.* **1999**, *31*, 498.

[23] Nigond, L.; Condamines, N.; Cordier, P. Y.; Livet, J.; Madic, C.; Cuillerdier, C.; Musikas, C. *Sep. Sci. Technol.* **1995**, *30*, 2075.

[24] Reinoso-García, M. M.; Verboom, W.; Reinhoudt, D. N.; Malinowska, E.; Pietrzak, M.; Wojciechowska, D. *Tetrahedron*, in press.

[25] Gutmann, V. *Coordination Chemistry in Non-Aqueous Solvents* Springer: New York, **1971**.

[26] Rowland, J. M.; Thornton, M. L.; Olmstead, M. M.; Mascharak, P. K. *Inorg. Chem.* **2001**, *40*, 1069.

[27] Bakker, E.; Bühlman, P.; Pretsch, E. *Chem. Rev.* **1997**, *97*, 3083.

[28] Wygladacz, K.; Malinowska, E.; Szczygelska-Tao, J.; Biernat, J. F. *J. Incl. Phenom.* **2001**, *39*, 309.

[29] Bakker, E.; Pretsch, E.; Bühlman, P. *Anal. Chem.* **2000**, *72*, 1127.

[30] (a) Mi, Y.; Bakker, E. *Anal. Chem.* **1999**, *71*, 5279; (b) Qin, Y.; Mi, Y.; Bakker, E. *Anal. Chim. Acta* **2000**, *421*, 207.

[31] Christensen, J. B. *Macromolecules* **2001**, *6*, 47.

Chapter 7

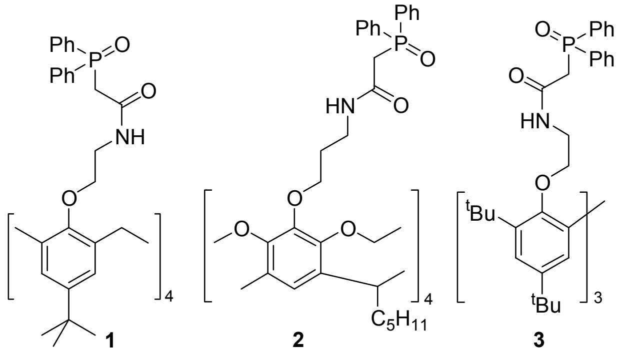
CMP(O) Tripodand Derivatives: Synthesis, Potentiometric Studies, and Extractions

Two ligand systems containing three carbamoylmethylphosphonate (CMP) or -phosphine oxide (CMPO) moieties attached to a tripodal platform have been synthesized for metal complexation and subsequent extraction from HNO_3 solutions. The incorporation into ion selective electrodes (ISE) and picrate extractions with Na^+, K^+, Ag^+, Ca^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, Cu^{2+}, Eu^{3+}, and Fe^{3+} shows that CMPO tripodand ***6*** *is very selective for Eu^{3+} and forms a very stable complex ($\log \beta_{ML} = 28.3$). Liquid-liquid extractions performed with Eu^{3+} and Am^{3+} reveal the good extraction properties of CMPO tripodand* ***6****, although much higher separation factors (>1000) were obtained with CMP tripodand* ***7****. Upon addition of the synergistic agent hexabrominated cobalt bis(dicarbollide) anion (Br_6-COSAN) the distribution coefficients for Am^{3+} and Eu^{3+} extraction increase up to 1000 for CMPO tripodand* ***6****. Covalently linked COSAN does not enhance the extraction of Am^{3+} and Eu^{3+}. The functionalization of dendrimer coated magnetic silica particles with CMP(O) tripodands led to very effective particles (****25*** *and* ***26****) for Am^{3+} and Eu^{3+} removal from 0.01M HNO_3 solutions.*

7.1 Introduction

In the previous Chapter the synthesis and binding properties of a series of tripodal compounds functionalized with *N*-acyl(thio)urea and picolin(thio)amide moieties towards different cations have been described. Unfortunately, these compounds are not good extractants of Am^{3+} and Eu^{3+}.

In this Chapter the synthesis and binding properties of carbamoylmethylphosphonate- (CMP) and phosphine oxide (CMPO) tripodand derivatives towards Na^+, K^+, Ag^+, Ca^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, Cu^{2+}, Fe^{3+}, Eu^{3+}, and Am^{3+} are described. As outlined before (Chapter 3) CMPO moieties are well known for the extraction of Am^{3+} and Eu^{3+} from nuclear waste.[1] Their attachment to platforms led to high extraction efficiencies and selectivities (Chart 7.1).[2,3,4,5] However, only one example of a tripodal platform with CMPO moieties has been reported so far (**3**).[6]



1 **2** **3**

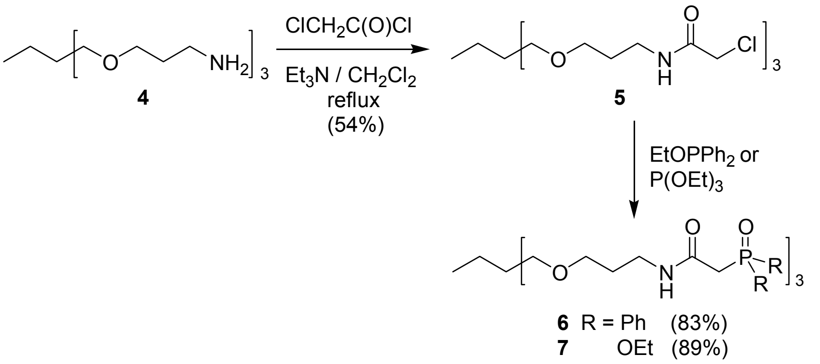
Chart 7.1.

Solvent extraction was used in previous Chapters for the removal of Am^{3+} from highly acidic solutions. The main problem involved in this process is the generation of large volumes of secondary waste. Nowadays, there are a few techniques, such as liquid membrane transport,[7] magnetically assisted chemical separation,[8] and extraction chromatography,[9] that are under investigation for the removal of actinides from HNO_3

solutions. The advantage of these techniques is that almost no secundary waste is generated. The last part of this Chapter deals with the use of CMP(O) tripodand derivatives on magnetic silica particles in magnetically assisted chemical separation.

7.2 Synthesis

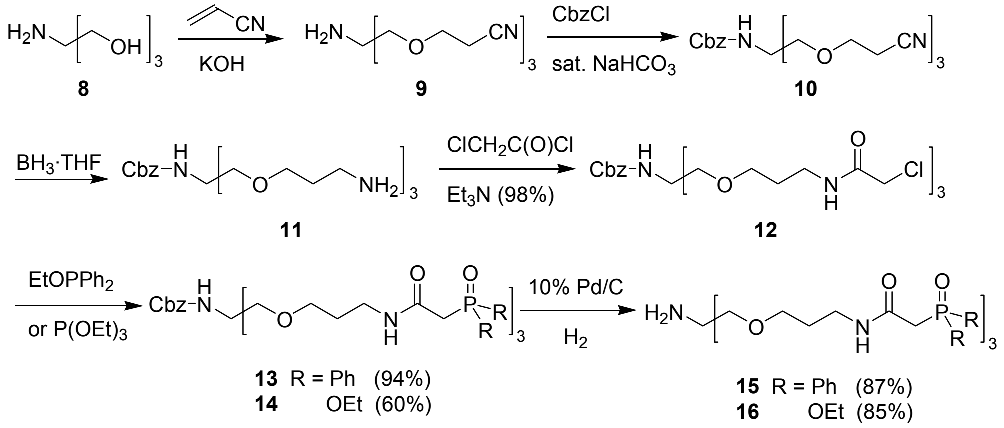
The synthesis of the tripodal CMP(O) compounds is depicted in Scheme 7.1. The ligating sites are introduced on the tripodal scaffold via two steps starting from 1,1,1-tris[(aminopropoxy)methyl]propane (**4**), the synthesis of which is described in Chapter 6. Acylation of amine **4** with chloroacetyl chloride and Et_3N as a base in CH_2Cl_2 afforded 1,1,1-tris[(chloroacetamidopropoxy)methyl]propane (**5**) in 54% yield. Arbusov reaction of **5** with ethyl diphenylphosphinite gave tris-[(diphenyl-carbamoylmethylphosphine oxide *N*-propoxy)methyl]propane (**6**) (CMPO tripodand) as a brown solid in 83% yield. Tris-[(diethyl-carbamoylmethylphosphonate *N*-propoxy)methyl]propane (**7**) (CMP tripodand) was obtained in 89% yield via an Arbusov reaction with triethyl phosphite.



Scheme 7.1.

The ^1H NMR spectra of CMPO tripodand **6** and CMP tripodand **7** exhibit characteristic signals for the CMP(O) methylene hydrogens at 3.40 ppm ($^2J_{PH}$=13.2 Hz) and 2.85 ppm ($^2J_{PH}$=20.8 Hz), respectively.

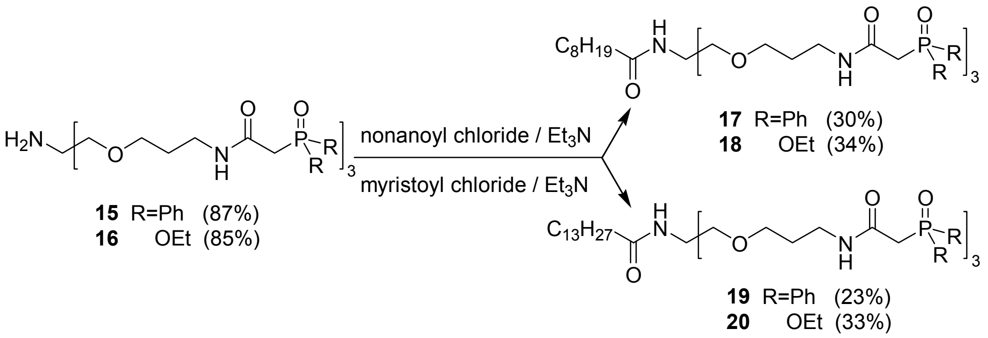
In order to introduce an extra functionality, which can be used as a handle for the coupling to COSAN moieties or magnetic silica particles, compound **11** was prepared following a literature procedure, starting from the commercially available 1,1,1-tris-(hydroxymethyl)aminomethane (**8**).[10] For the introduction of the CMP(O) moieties the same strategy as for CMP(O) tripodands **6** and **7** was followed. Acylation of carbamate **11** followed by an Arbusov reaction gave **13** and **14** in 94% and 60% yield, respectively. The terminal amino group, which was protected by the Cbz (benzyloxycarbonyl) group (**10**) just after the Michael addition of acrylonitrile to 1,1,1-tris-(hydroxymethyl)aminomethane (**8**), was deprotected by catalytic hydrogenation affording the target compounds **15** and **16** in 87% and 85% yield, respectively.



Scheme 7.2.

^{1}H NMR spectroscopy confirmed the formation of **15** and **16** by the absence of the signal at ~5.3 ppm of the CH_2 of the Cbz groups in **13** and **14**, and the presence of aromatic signals for CMPO tripodand **15** and ethylene of CMP tripodand **16.**

In order to increase the solubility of compounds **6** and **7**, especially CMP tripodand **7**, long alkyl chains were attached via the terminal amino group of CMP(O) tripodands **15** and **16**. The terminal amino group is at a sterically hindered position, which influences its reactivity. A nine carbon chain was introduced via an acylation reaction with nonanoyl chloride to give CMPO tripodand **17** and CMP tripodand **18** in 30 and 34% yield, respectively. CMP(O) tripodands **19** and **20**, which have a fourteen carbon chain, were obtained in 23% and 33% yield, respectively, by reaction of CMPO tripodand **15** and CMP tripodand **16** with myristoyl chloride. The formation of CMP(O) tripodands **17**-**20** was confirmed, in addition to the FAB mass spectra, by the appearance in the ^{1}H NMR spectra of two signals belonging to the alkyl chain, *viz*. a multiplet of the methylene groups at ~ 1.2-1.3 ppm and a triplet of the methyl groups at ~ 0.8 ppm.



Scheme 7.3.

7.3 Potentiometric measurements

In Chapter 6 potentiometric measurements with *N*-acyl(thio)urea- and picolin(thio)-amide-functionalized tripodands have been reported. Similar measurements were performed with compounds **6** and **7**. They were examined as ionophores in *o*-NPOE/PVC membranes containing also 30% mol of lipophilic anionic additives. The unbiased selectivity coefficients, $K_{I,J}^{pot}$, values were obtained in the same way as described in Chapter 6. The logarithmic values of the selectivity coefficients calculated for Pb^{2+} as the primary cation ($\log K_{i,j}^{pot}$) and Ag^+, Cu^{2+}, Cd^{2+}, and UO_2^{2+} are presented in Figure 7.1. These cations (Cd^{2+}, Pb^{2+}, and UO_2^{2+}) were selected for their presence in nuclear waste, as well as for their difference in charge and physical properties. Comparison of the results obtained for membranes containing CMPO tripodand **6**, CMP tripodand **7**, and for those membranes containing only ion-exchanger (KTFPB), revealed that the introduction of the ionophores in the membranes led to dramatic changes in the electrode selectivity for Pb^{2+} over Ag^{+}. CMP(O) tripodands **6** and **7** exhibit a high selectivity towards UO_2^{2+} and Pb^{2+} ions with selectivity coefficients, log K^{pot}_{Pb,UO_2}, of +4.5 and +2.2, respectively, indicating a higher selectivity for UO_2^{2+} than for Pb^{2+}. The selectivity found for UO_2^{2+} over Pb^{2+} ions for membranes based on **6** and **7** is much better than that reported for CMP(O) tetrakis-functionalized cavitands[11] (see Chapter 4).

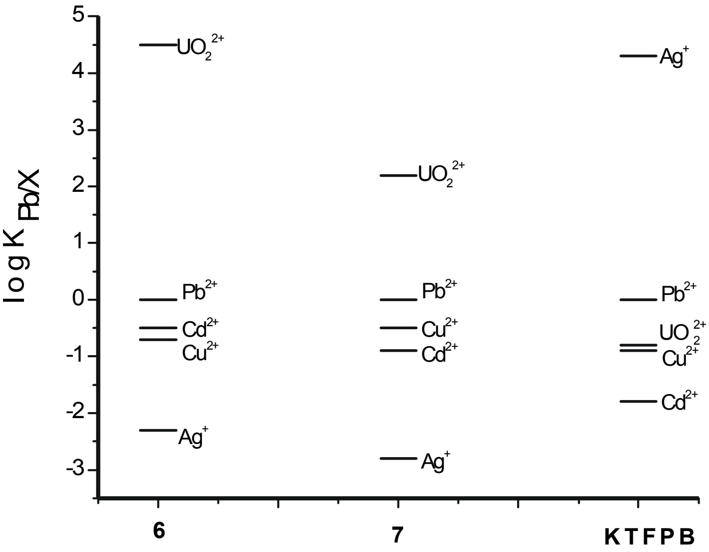


Figure 7.1. Selectivity coefficients for electrodes prepared with PVC/*o*-NPOE (1:2 by weight) membranes containing CMP(O) tripodands **6**, **7**, and liphophilic sites (KTFPB) as well as membranes with ion-exchanger only, with Pb^{2+} as the primary ion.

Complex formation constants were determined by means of the segmented sandwich method.[12] The values of the complex formation constants for ionophores **6** and **7** and selected cations are collected in Table 7.1. CMPO tripodand **6** forms stronger complexes than CMP tripodand derivative **7** with all the examined cations, following the expected trend of complexation properties for P-containing compounds: phosphine oxide > phosphate > phosphonate.[13] The largest complex formation constant, log β_{ML}, of CMPO tripodand **6** was found for Eu^{3+}, which was taken as a general representative for the trivalent actinides (Am^{3+} and Cm^{3+}) and lanthanides.

Table 7.1. Formal complex formation constants, log β_{ML}, obtained with ionophores **6** and **7** in PVC/*o*-NPOE (1:2) membranes, using the segmented sandwich method.

Ionophore / Cation	**6**	**7**
Ag^+	7.7	4.3
Cu^{2+}	19.8	11.8
Pb^{2+}	17.4	9.0
UO_2^{2+}	21.5	12.3
Eu^{3+}	28.3	7.9

7.4 Extraction experiments

7.4.1 Extraction of cations

To obtain initial insight into the extraction properties of the CMP(O) tripodands **6** and **7**, the extraction of a number of cations (Na^+, K^+, Ag^+, Ca^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, Cu^{2+}, Eu^{3+}, and Fe^{3+}) was investigated. In the extraction studies, Eu^{3+} was selected as a general representative for the trivalent actinides (*e.g.* Am^{3+} and Cm^{3+}) and lanthanides, while the other cations were selected for their difference in charge and physical properties. The results of the picrate extractions[14] are summarized in Figure 7.2.

The extraction percentages (%E values) reported in Figure 7.2 show that CMP tripodand **7** has a very similar extraction behavior towards the different cations used. CMPO tripodand **6** has a higher affinity for Eu^{3+} than for the other cations, having almost no affinity for Ag^+. The reason for this is that the CMPO ligating groups of **6** have hard donor atoms, while Ag^+ is a soft donor cation (Pearson's principle).[15]

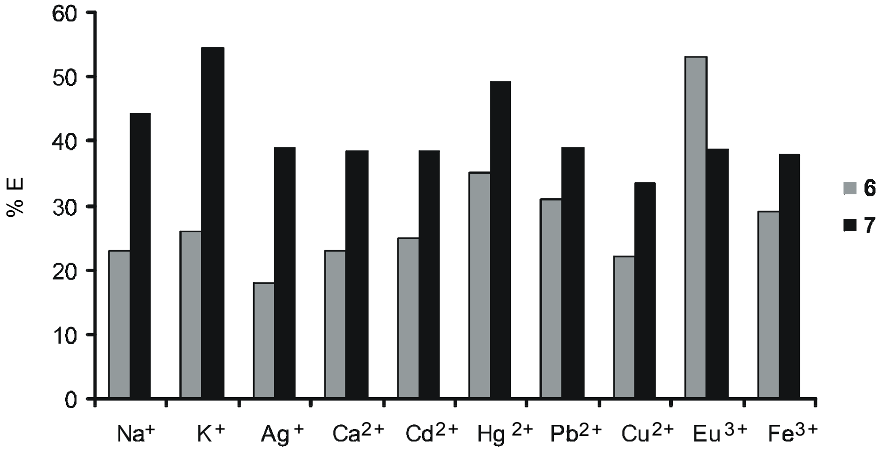


Figure 7.2. Extraction results of CMP(O) tripodands **6** and **7**.

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

7.4.2 Extraction of Lanthanides and Thorium

Extraction experiments of lanthanides and Th^{4+} were made to compare the results of CMP(O) tripodands **6** and **7** with the extraction data of CMPO-calix[4]arene **1** and CMPO-triphenoxymethane **3**, published in the literature, and CMPO-cavitand **2** reported in Chapter 3. The results of these extractions are summarized in Table 7.2. Unfortunately, the extraction efficiency of **7** could not be determined due to solubility problems.

Table 7.2. Extraction percentages (%E) of lanthanide and thorium nitrates from 1M HNO_3 into CH_2Cl_2 by CMPO bearing compounds **1**-**3** and **6** ($C_M=10^{-4}$M, volume organic phase / aqueous phase=1, T =20°C)[a]

Ionophore	La^{3+} $C_L=10^{-3}$M	Eu^{3+} $C_L=10^{-3}$M	Yb^{3+} $C_L=10^{-3}$M	Th^{4+} $C_L=10^{-4}$M
Calix[4]arene **1**[b]	19	16	3	76
Cavitand **2**[c]	13	12	7	81
Triphenoxymethane **3**[d]	4	3	10	40
Tripodand **6**	14	11	8	30

a) %E = 100% ($[M^{n+}]_{org}/[M^{n+}]_{tot}$) after extraction as determined by the Arsenazo(III) assay. Precision: $\pm\sigma_{n-1}$: 1 – 2.
b) Values taken from ref. 3.
c) Values taken from Chapter 3.
d) Values taken from ref. 6.

CMPO tripodand **6** has about the same extraction profile for the different lanthanides as CMPO-calixarene **1** and CMPO-cavitand **2**. However, CMPO tripodand **6** does not have selectivity for Th^{4+}. This may be explained by the proximity of its chelating arms, which is great in the cases of CMPO-calix[4]arene **1** and CMPO-cavitand **2**. The results obtained with CMPO tripodand **6** are somewhat better, in case of the lanthanides, than those reported for tripodal triphenoxymethane **3**. However, the lanthanides *vs* thorium extraction ratio is lower. As is the case for **3**, the higher affinity of **6** for Th^{4+} than for lanthanides may be attributed to the higher intrinsic stability of the thorium complex created by the combined effects of its increased Lewis acidity relative to the trivalent lanthanides and the increased ability of the actinide metal to accommodate the coordination environment presented by the ligand.[6]

7.4.3 Extraction of Americium and Europium

Extraction experiments of Am^{3+} and Eu^{3+} were performed as in Chapter 3, with *o*-nitrophenyl hexyl ether (NPHE) as the organic phase at varying nitric acid concentrations. The results of these extractions are reported in Table 7.3.

Table 7.3. Distribution coefficients and separation factors ($S_{Am/Eu}$) for the extraction of Eu^{3+} and Am^{3+} by CMP(O) tripodands **6** and **7**.[a]

Ionophore	Cation	HNO_3 concentration					
		0.001M	0.01M	0.1M	1M	2M	4M
6 (10^{-3}M)	Eu^{3+}	16.84	4.11	0.68	1.11	1.68	2.98
	Am^{3+}	89.16	7.57	1.37	2.74	3.86	5.50
	$S_{Am/Eu}$	*5.3*	*1.8*	*2.0*	*2.5*	*2.3*	*1.8*
7[b] (5.10^{-4}M)	Eu^{3+}	0.40	0.01	0.02	0.01	0.03	0.12
	Am^{3+}	31	7	11	9	21	27
	$S_{Am/Eu}$	*77*	*524*	*574*	*1042*	*744*	*225*

a) Aqueous phase: 152-Eu; 241-Am / [HNO_3] variable (~1500 kBq/L)/(Sp Gamma D3/0.5 mL). Organic phase: ligand (10^{-3}M) in NPHE.
b) Major precipitation at all the acidities. No decimals were taken due to the high error found.

CMPO tripodand **6** has a very high extraction efficiency at 0.001M HNO_3 with $S_{Am/Eu}$=5.3. In general, the results are much better than those obtained with the CMPO-cavitands reported in Chapter 3, the separation factors of which were ≤ 2 and of which distribution coefficients were not higher than 32 (in the same HNO_3 concentration range). The best extraction results and a pronounced selectivity for Am^{3+} over Eu^{3+} were obtained with CMP tripodand **7**, with distribution coefficients between 7 and 31 in the HNO_3 concentration range used. Its separation factors are remarkable, up to 1042 at 1M HNO_3. However, these results have to be considered very carefully due to the formation of a third phase.

In the case of CMPO tripodand **6** the extractions were also performed in the presence of hexabrominated cobalt bis(dicarbollide) anion (Br_6-COSAN) as a synergist. The results reported in Table 7.4 show an enhancement of the extraction efficiency of the CMPO tripodand **6** in comparison with the results obtained without Br_6-COSAN (Table 7.3), especially at low HNO_3 concentrations. These results are in perfect agreement with the results obtained in previous Chapters (Chapters 3, 5, and 6).

Table 7.4. Distribution coefficients and separation factors ($S_{Am/Eu}$) for the extraction of Eu^{3+} and Am^{3+} by CMPO tripodand **6** in the presence of Br_6-COSAN as a synergist.[a]

	HNO_3 concentration					
Cation	0.001M	0.01M	0.1M	1M	2M	3M
Eu^{3+}	>1000	>1000	>1000	56.0	14.8	8.4
Am^{3+}	>1000	>1000	>1000	76.6	25.8	13.1
$S_{Am/Eu}$	*n.d.*[b]	*n.d.*[b]	*n.d.*[b]	*1.4*	*1.7*	*1.6*

a) Aqueous phase: 152- Eu; 241-Am / [HNO_3] variable (~1500 kBq/L)/(Sp Gamma D3/0.5 mL).
Organic phase: **1** (10^{-3}M) + Br_6-COSAN (3.10^{-3}M) in NPHE.
b) Not determined.

In order to avoid third phase formation, as in the case of CMP tripodand **7**, similar extractions were performed from 1M HNO_3 into tetrachloroethane (TCE) with CMP(O) tripodands **6**, **7**, **17**, **18**, **19**, and **20**. CMP(O) tripodands **17**-**20** have a long alkyl chain to enhance the solubility. However, CMP tripodands **7**, **18**, and **20** form precipitates when dissolved in TCE and contacted with acidic aqueous solutions.

Table 7.5 shows the Eu^{3+} and Am^{3+} extraction data of the CMPO tripodands **6**, **17**, and **19**. CMPO tripodand **17**, which has a nonanoyl chain, presents the best distribution coefficients. Within the three CMPO tripodands **6**, **17**, and **19**, **6** has the highest separation factor ($S_{Am/Eu}$=2.2). It is on the same order of magnitude as that obtained in the experiments performed in NPHE as a solvent and at the same HNO_3 concentration (see Table 7.3). This shows that the introduction of a long alkyl chain does not enhance the extraction properties of CMPO tripodand **6** (**6** *vs* **17** and **19**). Compared to malonamides used in the DIAMEX process (0.65M *N*,*N'*-dimethyl-*N*,*N'*-dioctyl-2-hexylethoxymalonamide (DMDOHEMA) in hydrogenated tetrapropene (TPH) at 1M HNO_3), with D_{Am}=0.2 and D_{Eu}=0.1, CMPO tripodands **6**, **17**, and **19** are better extracting agents of Eu^{3+} and Am^{3+}.

Table 7.5. Distribution coefficients and separation factors for the extraction of Eu^{3+} and Am^{3+} by CMPO tripodands **6**, **17**, and **19**.[a]

Cation	Ionophore		
	6	**17**	**19**
Eu^{3+}	1.0	2.2	1.0
Am^{3+}	2.2	4.1	1.7
$S_{Am/Eu}$	*2.2*	*1.9*	*1.7*

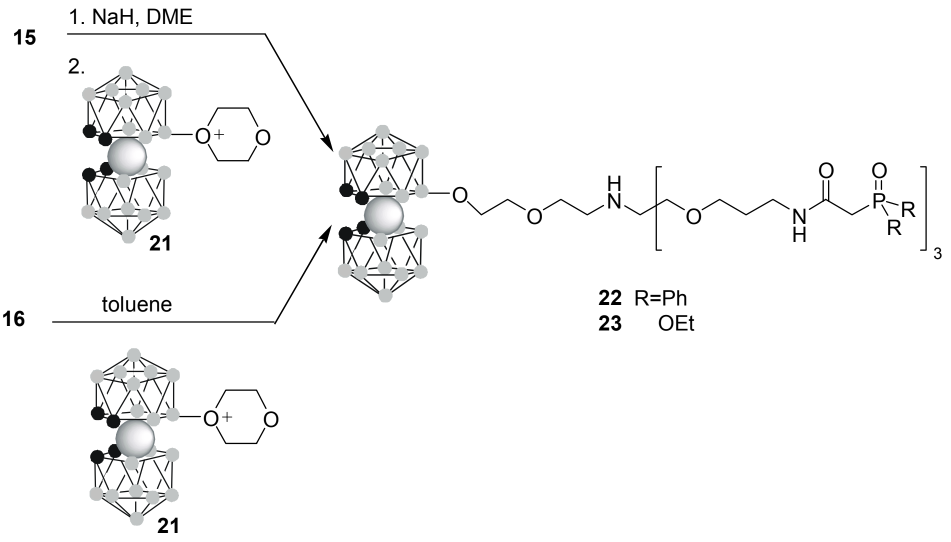
a) Aqueous phase: 152-Eu and 241-Am trace level in 1M [HNO_3].
Organic phase: ligand (**6** 10^{-2}M, **17** 1.7 10^{-2}M, and **19** 1.2 10^{-2}M) in TCE.

More diluted TCE solutions of the CMP tripodands **7**, **18**, and **20** were also tested to prevent third phase formation. Even at a low concentration of 6.8 10^{-4}M CMP tripodand **7** could not be measured due to the appearance of a precipitate, when the organic layer is mixed with the HNO_3 solution. However, in the case of compound **18**, at a ligand concentration of 5.6 10^{-4}M in TCE, extraction of Am^{3+} and Eu^{3+} from 0.1-3M HNO_3 was possible, although the distribution coefficients were very low (1.1 10^{-3}-3.9 10^{-3}). The extraction efficiency of CMP tripodand **20** could be measured at a somewhat higher concentration (1.9 10^{-3}M) to give distribution coefficients for Eu^{3+} and Am^{3+} of 2.1 10^{-3} and 3 10^{-3}, respectively, at 3M HNO_3 (precipitation occurred at lower concentrations).

CMPO tripodand **17** presents somewhat higher distribution coefficient values for Am^{3+} and Eu^{3+} and a similar separation factor as CMPO tripodand **6**. However, in general, the results obtained with CMP(O) tripodands **17**-**20** show that the introduction of long alkyl chains to CMP(O) tripodands **6** and **7** does not change their extraction properties.

7.5 COSAN moieties covalently linked to CMP(O) tripodands

In order to enhance the extraction ability of CMP(O) tripodands **6** and **7**, as well as the solubility in the case of **7**, cobalt bis(dicarbollide) anions (COSAN) were covalently attached to amino terminated CMP(O) tripodands **15** and **16** to give **22** and **23** by the group of Dr. Grüner at the Institute of Inorganic Chemistry of the Academy of Sciences (Czech Republic) (Scheme 7.4).



Scheme 7.4.

Extraction experiments of Am^{3+} and Eu^{3+} from HNO_3 solutions were performed with COSAN-containing CMP(O) tripodands **22** and **23**. CMPO derivative **22** gave low distribution coefficients, D_{Am}=0.4 and D_{Eu}=0.3 (1M **22** in toluene, 0.1M HNO_3). The distribution coefficients for Eu^{3+} with 1M COSAN-containing CMP tripodand **23** in nitrobenzene at 0.1 and 1M HNO_3, are 311 and 4.55, respectively. The attachment of

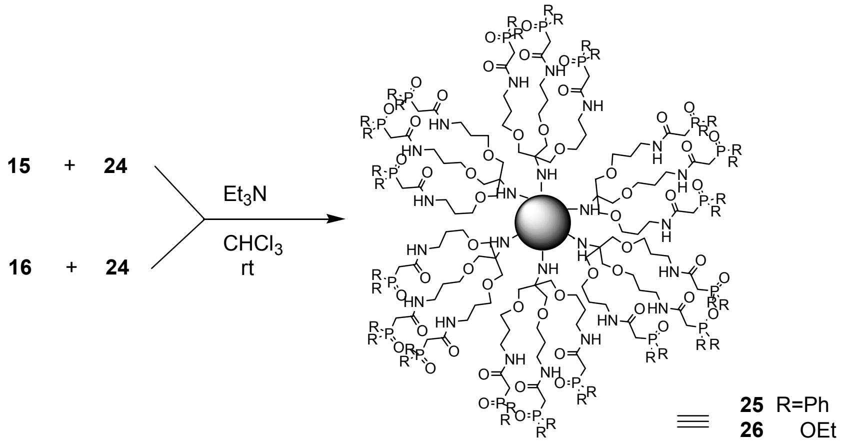
COSAN moieties to the CMP(O) tripodand derivatives, **22** and **23**, does not have the same effect as in the case of the COSAN-containing cavitand derivatives (Chapter 5), extraction properties of which were better than their analogues without COSAN. Probably the secondary amine is protonated under the acidic conditions and consequently compounds **22** and **23** are not negatively charged. However, the linkage of COSAN to the CMP tripodand **23** makes it more soluble and no precipitation was formed during the Eu^{3+} extraction experiments.

7.6 CMP(O) tripodand-containing magnetical particles

In the introduction it was mentioned that recently a new separation technology was introduced for nuclear waste treatment, *viz.* magnetically assisted chemical separation with extractant coated particles. It combines the selectivity of a ligand used for liquid-liquid extractions with improved phase separation due to the magnetic field, resulting in an effective system that provides only a small volume of high level waste. The magnetic particles can be directly vitrified or stripped, to enable their re-use in an automated process. Fundamental studies have been performed by Nuñez and Kaminski et al.[16,17,18] The better extraction properties (~12-fold)[19,20] obtained with calix[4]arenes bearing four CMPO groups covalently bound to the particle surface in comparison with particles with adsorbed CMPO moieties, inspired our alternative strategy of covalent attachment of CMP(O) tripodal ionophores on the surface of magnetic particles for Eu^{3+}/Am^{3+} separation from high activity liquid wastes.

In order to achieve a further increase of the lanthanide and actinide extraction capacity of functionalized magnetic particles, starburst dendrimers have been introduced on the particle surface. These dendrimer coated magnetic particles have a high potential for immobilization of a large variety of selective chelators in a very high density on the particle surface.[21] The extraction studies for Eu^{3+} and Am^{3+} were carried out under highly acidic conditions with Eu^{3+} and Am^{3+} solutions found in real waste.

CMP(O) tripodand-containing magnetical particles were prepared by reaction of CMP(O) tripodands **15** and **16** with magnetical particles functionalized with 3rd generation dendrimers **24** at Micromod Partikeltechnologie GmbH (Scheme 7.5).



Scheme 7.5.

The distribution coefficient K_D for solid/liquid extractions is defined as:

$$K_D = \frac{(C_{L,0} - C_L)}{C_L} \cdot \frac{V_L}{m_s}$$

Due to saturation phenomena, these K_D values are usually not constant and thus only values obtained under identical conditions (concentration in the liquid phase, amount of solid phase) can be compared. Therefore the distribution coefficients (K_D) for Eu^{3+} and Am^{3+} extraction with magnetic particles (m_s) with 10 mL (V_L) of Eu^{3+} or Am^{3+} containing test solution of known activity (C_L) were measured in the supernatant. The results of the extraction experiments with CMP(O) tripodand modified particles **25** and **26** towards Am^{3+} and Eu^{3+} are given in Table 7.6.

The CMPO tripodand bearing particles **25** are very effective for Eu^{3+} and Am^{3+} at 0.01M HNO_3 and have a selectivity factor of 3.7 at 0.1M HNO_3. CMP tripodand bearing particles **26** are not so effective as **25**, but they have a higher separation factor at 0.01M HNO_3 (2.5 *vs* 1 for **25**). At HNO_3 concentrations higher than 0.01M the distribution coefficients decrease to values lower than 1, abruptly in the case of CMP tripodand bearing particles **26**, and gradually for CMPO tripodand bearing particles **25**. The distribution coefficients for CMPO tripodand bearing particles **25** at 3M HNO_3 are much lower than those reported for simple CMPO-bearing particles (K_D=23 and 48 for Eu^{3+} and Am^{3+}, respectively).[22] However, the high distribution coefficients of the CMPO tripodand bearing particles at low HNO_3 concentrations constitute a system for future potential industrial development.

Table 7.6. Distribution coefficients for the extraction of Am^{3+} and Eu^{3+} by microparticles **25** and **26** bearing CMP(O) tripodands on the surface.[a]

Particle type	Cation	HNO_3 concentration			
		0.01M	0.1M	1M	3M
25	Eu^{3+}	1215	221	1.5	<1
	Am^{3+}	1359	59	2.1	<1
26	Eu^{3+}	102	<1	<1	<1
	Am^{3+}	256	<1	<1	<1

a) Extraction conditions: Aqueous phase: 10 mL of HNO_3 + 152-Eu + 241-Am; mass of particles 300 mg; stirring time: 1 h.

7.7 Conclusions

C$_3$-symmetric tris-CMP(O) ligand systems **6**, **7**, **15**-**20** were developed. By liquid-liquid extractions and ISE data it has been demonstrated that CMPO tripodand **6** has a higher affinity for actinides (UO_2^{2+}, Am^{3+}) and Eu^{3+} than CMP tripodand **7**, having a very high complex formation constant for Eu^{3+} ($\log \beta_{ML}$ =28.3).

Upon addition of the synergistic agent hexabrominated cobalt bis(dicarbollide) anion (Br_6-COSAN) the distribution coefficients for Am^{3+} and Eu^{3+} extraction of CMPO tripodand **6** increase up to 1000-fold. However, the attachment of COSAN to CMP(O) tripodands **15** and **16** gives rise to uncharged species under acidic conditions (**22** and **23**), and as a result the extraction properties are not improved.

Dendrimer-coated magnetic silica particles functionalized on the surface with CMPO tripodand **25** have high distribution coefficients for Am^{3+} and Eu^{3+} extraction at low HNO_3 concentration, which may make it a promising system for industrial development.

7.8 Experimental part

General

^1H and ^{13}C NMR spectra were recorded on 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 an internal standard and chemical shifts are given in ppm relative to tetramethylsilane (TMS). Fast atom bombardment (FAB) mass spectra were measured on a Finnigan MAT 90 spectrometer using *m*-nitrobenzyl alcohol (NBA) as a matrix. Matrix-Assisted Laser Desorption Ionisation Time-of-Flight (MALDI-TOF) mass spectra were recorded using a Perkin Elmer/PerSpective Biosystems Voyager-DE-RP MALDI-TOF mass spectrometer. Elemental analyses were carried out using a 1106 Carlo-Erba Strumentazione element analyser. 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. Melting points (uncorrected) of all compounds were obtained on a Reichert melting point apparatus.

Compounds **4**[23] and **11**[10] were prepared following a literature procedure.

Potentiometric measurements and picrate extractions were performed as described in Chapter 4. Extraction of lanthanides and Th^{4+} and Am^{3+} and Eu^{3+} with CMP(O) tripodands **6** and **7** was performed as described in Chapter 3. Extractions of Am^{3+} and Eu^{3+} with COSAN-containing CMP(O) tripodand compounds **22** and **23** were done as in Chapter 5.

1,1,1-Tris[(chloroacetamidopropoxy)methyl]propane 5

To a solution of 1,1,1-tris[(aminopropoxy)methyl]propane **4** (865 mg, 2.84 mmol) and Et_3N (6.4 mL, 45.6 mmol) in CH_2Cl_2 (50 mL) was added chloroacetyl chloride (2.75 mL, 34.6 mmol), and the reaction mixture was heated at reflux overnight. The solution was washed with 1M HCl (2 × 25 mL), H_2O (2 × 25 mL), 2M NaOH (3 × 25 mL) and 1M HCl (2 × 25 mL) and dried over $MgSO_4$. Evaporation of the solvent afforded **5** as a pale yellow oil. Yield 813 mg (54%); FAB-MS: *m/z* 535.4 ($[M+H]^+$, calcd 535.1); ^1H NMR δ 6.96-6.98 (m, 3H, NH), 4.06 (s, 6H, CH_2Cl), 3.50 (t, 6H, *J*=6.0 Hz, OCH_2), 3.43 (q, 6H, *J*=6.0 Hz, CH_2NH), 3.34 (s, 6H, CCH_2O), 1.82 (q, 6H, *J*=6.0 Hz, CH_2), 1.46 (q, 2H, *J*=7.7 Hz CH_2), 0.85 (t, 3H, *J*=7.7 Hz, CH_3); ^{13}C NMR δ 165.8, 71.8, 70.0, 42.7, 38.2, 37.9, 29.1, 23.2, 7.7.

1,1,1-Tris[(diphenyl-carbamoylmethylphosphine oxide *N*-propoxy)methyl]propane 6

In an open flask compound **5** (933 mg, 1.25 mmol) was dissolved in a small amount of ethyl diphenylphosphinite (1 mL, 4.125 mmol) while the temperature was gradually increased from 100°C to 150°C, whereupon the mixture was stirred for 1 h at 150°C. After cooling of the reaction mixture diisopropyl ether was added till a precipitate was formed. The precipitate was filtered off and dissolved in CH_2Cl_2 in order to take all the compound from the filter. The organic solvent was removed in vacuo yielding **6** as a light brown solid. Yield 1.07 g (83%); mp 68-70°C; FAB-MS: *m/z* 1032.7 ($[M+H]^+$, calcd 1032.4); ^1H NMR δ 7.70-7.82 and 7.45-7.51 (2m, 12+18H, P-phenyl), 3.40 (6, 6H, *J*=13.2 Hz, CH_2P), 3.21-3.31 (m, 12H, OCH_2+CH_2NH), 3.15 (s, 6H, CCH_2O), 1.62 (q, 6H, *J*=6.6 Hz, CH_2), 1.33 (q, 2H, *J*=7.3 Hz, CH_2), 0.79 (t, 3H, *J*=7.3 Hz, CH_3); ^{13}C NMR δ 162.0, 132.0, 131.0, 130.0, 128.0, 71.0, 68.0, 42.0, 39.0, 38.0, 37.5, 36.0, 22.5, 7.0; Anal. calcd for $C_{57}H_{68}N_3O_9P_3\cdot 1/2CH_2Cl_2$: C, 64.27; H, 6.47; N, 3.91 Found: C, 64.76; H, 6.17; N, 3.82.

1,1,1-Tris[(diethyl-carbamoylmethylphosphonate *N*-propoxy)methyl]propane 7

In an open flask compound **5** (813 mg, 1.52 mmol) was dissolved in a small amount of triethyl phosphite (0.86 mL, 5.01 mmol) while the temperature was gradually increased from 100°C to 150°C, and the mixture was stirred for 1 h at 150°C. After cooling of the reaction mixture, diisopropyl ether was added and the mixture left stirring overnight. The organic solution was decanted remaining a brown oil. Yield 1.13 g (89%). FAB-MS: *m/z* 839.4 ($[M+H]^+$, calcd 839.0); ^1H NMR δ 4.16 (q, 12H, *J*=7.1 Hz, OCH_2), 3.46 (t, 6H, *J*= 6.0 Hz, OCH_2), 3.35 (q, 6H, *J*=6.0 Hz, CH_2NH), 3.27 (s, 6H, CCH_2O), 2.85 (d, 6H, *J*=20.8 Hz, CH_2P), 1.78 (q, 6H, *J*=6.0 Hz, CH_2), 1.36-1.20 (m, 18+2H, CH_3+CH_2), 0.84 (t, 3H, *J*=7.1 Hz, CH_3); ^{13}C NMR δ 163.0, 71.0, 68.0, 62.0, 42.5, 37.0, 36.0, 34.0, 28.5, 22.5, 18.0, 7.5.

Cbz-chloroacetamido-tripodand 12

To a solution of carbamate **11** (526 mg, 1.23 mmol) and Et_3N (2.2 mL, 16 mmol) in CH_2Cl_2 (35 mL) was added chloroacetyl chloride (1.27 mL, 12.3 mmol), and the reaction mixture was refluxed overnight. The solution was washed with 1M HCl (2 × 20 mL), H_2O (2 × 20 mL), 2M NaOH (3 × 20 mL) and 1M HCl (2 × 20 mL) and dried over $MgSO_4$. Evaporation of the solvent afforded **12** as a pale yellow oil. Yield 795 mg (98%); FAB-MS: *m/z* 657.5 ($[M+H]^+$, calcd 657.3); ^1H NMR δ 7.33 (s, 5H, ArH), 6.97-6.99 (m, 3H, NH), 5.03 (s, 2H, CH_2), 4.06 (s, 6H, CH_2Cl), 3.69 (s, 6H, CCH_2O), 3.51 (t, 6H, *J*=5.8 Hz, OCH_2), 3.37 (q, 6H, *J*=5.8 Hz, CH_2NH), 1.77 (q, 6H, *J*=5.8 Hz, CH_2); ^{13}C NMR δ 165.6, 154.6, 135.1, 127.9, 127.51, 69.4, 65.8, 58.1, 42.1, 37.4, 28.4.

Cbz-CMPO-tripodand 13

In an open flask compound **12** (300 mg, 0.76 mmol) was dissolved in a small amount of ethyl diphenylphosphinite (0.6 mL, 5.0 mmol) while the temperature was gradually increased from 100°C to 150°C, and the mixture was stirred for 1 h at 150°C. After cooling of the reaction mixture diisopropyl ether was added till a precipitate was formed. The precipitate was filtered off and dissolved in CH_2Cl_2 in order to collect all product from the filter. The organic solvent was evaporated yielding **13** as a light brown solid. Yield 703 mg (94%); mp 58-60°C; FAB-MS: *m/z* 1153.5 ($[M+H]^+$, calcd 1153.0); ^1H NMR δ 7.70-7.80 and 7.42-7.54 (2m, 12+18H, P-phenyl), 7.28 (s, 5H, Ar), 5.32 (s, 2H, OCH_2Ar), 3.65 (s, 6H, CCH_2O), 3.35 (t, 6H, *J*=6.0 Hz, OCH_2), 3.30 (d, 6H, *J*=13.2 Hz, CH_2P), 3.25 (q, 6H, *J*=6.0 Hz, CH_2NH), 1.62 (q, 6H, *J*=6.0 Hz, CH_2); ^{13}C NMR δ 164.6, 155.5, 136.8, 132.2, 131.0, 130.8, 128.8, 128.7, 128.5, 128.4, 69.6, 69.3, 65.3, 46.2, 38.6, 37.5, 29.2; Anal. calcd for $C_{63}H_{71}N_4O_{11}P_3\cdot 1/2CH_2Cl_2$: C, 63.79; H, 6.07; N, 4.69 Found: C, 63.30; H, 5.93; N, 4.23.

Cbz-CMP-tripodand 14

In an open flask compound **12** (500 mg, 0.76 mmol) was dissolved in a small amount of triethyl phosphine (0.86 mL, 5.01 mmol) while the temperature was gradually increased from 100°C to 150°C, and the mixture was stirred for 1 h at 150°C. After cooling of the reaction mixture diisopropyl ether was added and left stirring overnight. The organic solution was decanted leaving compound **14** as a brown oil. Yield 438 mg (60%). FAB-MS: *m/z* 962.3 ($[M+H]^+$, calcd 962.4); ^1H NMR δ 7.31 (s, 5H, ArH), 5.29 (s, 2H, OCH_2Ar), 4.10 (q, 12H, *J*=7.1 Hz, OCH_2), 3.66 (s, 6H, CCH_2O), 3.49 (t, 6H, *J*=5.5 Hz, OCH_2), 3.31 (q, 6H, *J*=5.5 Hz, 6H, CH_2NH), 2.79 (d, 6H, *J*=20.8 Hz, CH_2P), 1.74 (q, 6H, *J*=5.5 Hz, CH_2), 1.29 (t, 18H, *J*=7.1 Hz, CH_3); ^{13}C NMR δ 163.5, 154.9, 135.9, 127.8, 127.4, 69.2, 68.8, 65.6, 61.9, 58.3, 36.9, 33.6, 28.4, 15.7.

Amino-CMPO-tripodand 15

A suspension of compound **13** (632 mg, 0.64 mmol) and 10% Pd/C (98 mg) in MeOH (25 mL) was stirred under a hydrogen atmosphere overnight. The product was filtered over celite and washed thoroughly with MeOH, and removal of the solvent gave a solid which was redisolved in CH_2Cl_2. Evaporation of CH_2Cl_2 yielded **15** as a light yellow solid. Yield 500 mg (87%); mp 70-72°C; MALDI-MS: *m/z* 1019.4 ($[M+H]^+$, calcd 1019.0); ^1H NMR δ 7.70-7.80 and 7.42-7.54 (2m, 12+18H, P-phenyl), 3.64 (s, 6H, CCH_2O), 3.36-3.39 (m, 6H, OCH_2), 3.30 (d, 6H, *J*=13.2 Hz, CH_2P), 3.24-3.28 (m, 6H, CH_2NH), 1.62 (q, 6H, *J*=5.7 Hz, CH_2); ^{13}C NMR δ 164.2, 131.2, 130.8, 128.8, 128.0, 69.9, 62.8, 59.0, 37.7 , 37.2, 29.1, 28.4; Anal. calcd for $C_{55}H_{65}N_4O_9P_3 \cdot 3/4CH_2Cl_2$: C, 61.84; H, 6.19; N, 5.17 Found: C, 62.15; H, 5.82; N, 5.43.

Amino-CMP-tripodand 16

A suspension of compound **14** (185 mg, 0.19 mmol) and 10% Pd/C (98 mg) in MeOH (20 mL) was stirred under a hydrogen atmosphere overnight. The product was filtered over celite and washed thoroughly with MeOH, and removal of the solvent gave **16** as a brown oil. Yield 135 mg (85%); MALDI-MS: *m/z* 827.2 ($[M+H]^+$, calcd 827.0); ^1H NMR δ 4.16 (q, 12H, *J*=7.1 Hz, OCH_2), 3.65 (s, 6H, CCH_2O), 3.58 (t, 6H, *J*=5.5 Hz, OCH_2), 3.42 (q, 6H, *J*=5.5 Hz, CH_2NH), 3.05 (d, 6H, *J*=21.2 Hz, CH_2P), 1.74 (q, 6H, *J*=5.5 Hz, CH_2), 1.35 (t, 18H, *J*=7.1 Hz, CH_3); ^{13}C NMR δ 164.2, 70.4, 63.0, 62.7, 37.9, 34.3, 28.4, 16.3.

General procedure for the synthesis of tripodands 17-20

A solution of compounds **15** or **16**, nonanoyl chloride or myristoyl chloride and Et_3N (1.1 equiv) in CH_2Cl_2 (25 mL) was refluxed for 24 h. Upon cooling the solution was sequentially washed with a saturated solution of NH_4Cl (2 × 25 mL), H_2O (2 × 25 mL), 2M NaOH (3 × 25 mL), and a saturated solution of NH_4Cl (2 × 25 mL), and dried over $MgSO_4$. Evaporation of the solvent afforded the desired compounds. Final purification was by preparative TLC (SiO_2, AcOEt/MeOH, 95/5; the target compounds remain at the bottom of the plate). The compounds were removed from the silica with CH_2Cl_2. Evaporation of the solvent gave the pure compounds **17-20**.

Nonanoyl-CMPO-tripodand 17 The general procedure was applied to **15** (145 mg, 0.14 mmol), nonanoyl chloride (0.03 mL, 0.15 mmol), and Et_3N (0.02 mL, 0.15 mmol) to give compound **17** as a light brown solid. Yield 49 mg (30%); mp 64-66°C; FAB-MS: *m/z* 1181.0 ($[M+Na]^+$, calcd 1181.5); ^1H NMR δ 7.62-7.72 and 7.31-7.46 (2m, 12+18H, P-phenyl), 3.55 (s, 6H, CCH_2O), 3.15-3.31 (m, 18H, OCH_2+CH_2P+CH_2NH), 2.05-2.10 (m, 2H, CH_2), 1.53 (q, 6H, *J*=5.8 Hz, CH_2), 1.13-1.20 (m, 12H, CH_2), 0.80 (t, 3H, *J*=6.6 Hz, CH_3); ^{13}C NMR δ 164.0, 130.8, 129.4, 129.3, 127.1, 126.9, 69.6, 69.3, 68.7, 39.2, 38.6, 37.0, 30.0, 27.8, 21.7, 14.1; Anal. calcd for $C_{64}H_{81}N_4O_{10}P_3 \cdot 2CH_2Cl_2$: C, 59.64; H, 6.45; N, 4.22 Found: C, 59.35; H, 6.35; N, 3.92.

Nonanoyl-CMP-tripodand 18 The general procedure was applied to **16** (183 mg, 0.22 mmol), nonanoyl chloride (0.044 mL, 0.24 mmol), and Et_3N (0.03 mL, 0.24 mmol) to give compound **18** as a brown oil. Yield 73 mg (34%); FAB-MS: *m/z* 989.6 ($[M+Na]^+$, calcd 989.0); ^1H NMR δ 4.07 (q, 12H, *J*=7.1 Hz, OCH_2), 3.63 (s, 6H, CCH_2O), 3.43 (t, 6H, *J*= 5.9 Hz, OCH_2), 3.28 (q, 6H, *J*=5.9 Hz, 6H, CH_2NH), 2.80 (d, 6H, *J*=20.8 Hz, CH_2P), 2.1 (t, 2H, *J*=6.9 Hz, CH_2), 1.68 (q, 6H, *J*=5.9 Hz, CH_2), 1.27 (t, 18H, *J*=7.1 Hz, CH_3), 1.18-1.19 (m, 12H, CH_2), 0.80 (t, 3H, *J*=6.9 Hz, CH_3); ^{13}C NMR δ 164.2, 69.8, 69.2, 62.6, 59.7, 37.4, 35.8, 34.5, 31.8, 29.4, 29.2, 25.8, 22.6, 16.4, 14.0.

Myristoyl-CMPO-tripodand 19 The general procedure was applied to **15** (147 mg, 0.14 mmol), myristoyl chloride (0.04 mL, 0.16 mmol), and Et_3N (0.02 mL, 0.16 mmol) to give compound **19** as a light brown solid. Yield 40 mg (23%); mp 60-62°C; FAB-MS: *m/z* 1229.8 ([M+H]$^+$, calcd 1229.6); ^{1}H NMR δ 7.68-7.61 and 7.35-7.42 (2m, 12+18H, P-phenyl), 3.55 (s, 6H, CCH_2O), 3.31 (t, 6H, *J*=6.2 Hz, OCH_2), 3.22 (d, 6H, *J*=13.6 Hz, CH_2P), 3.16 (q, 6H, *J*=6.2 Hz, CH_2NH), 1.82-2.00 (m, 2H, CH_2), 1.53 (q, 6H, *J*=6.2 Hz, CH_2), 1.13-1.18 (m, 22H, CH_2), 0.80 (t, 3H, *J*=6.5 Hz, CH_3); ^{13}C NMR δ 164.6, 132.3, 130.9, 130.8, 128.8, 128.7, 69.6, 69.3, 68.7, 39.2, 38.6, 37.0, 31.8, 29.2, 22.6, 14.1; Anal. calcd for $C_{69}H_{91}N_4O_{10}P_3{\cdot}5/4CH_2Cl_2$: C, 63.18; H, 7.06; N, 4.91 Found: C, 63.20; H, 6.85; N, 4.73.

Myristoyl-CMP-tripodand 20 The general procedure was applied to **16** (135 mg, 0.16 mmol), myristoyl chloride (0.045 mL, 0.18 mmol), and Et_3N (0.025 mL, 0.18 mmol) to give compound **20** as a brownish oil. Yield 56 mg (33%); FAB-MS: *m/z* 1024.6 ([M+Na]$^+$, calcd 1024.0); ^{1}H NMR δ 4.16 (q, 12H, *J*=6.9 Hz, OCH_2), 3.72 (s, 6H, CCH_2O), 3.50 (t, 6H, *J*= 5.8 Hz, OCH_2), 3.28 (q, 6H, *J*=5.8 Hz, CH_2NH), 2.88 (d, 6H, *J*=20.8 Hz, CH_2P), 2.16-2.19 (m, 2H, CH_2), 1.68 (q, 6H, *J*=5.8 Hz, CH_2), 1.37 (t, 18H, *J*=6.9 Hz, CH_3), 1.25-1.27 (m, 22H, CH_2), 0.89 (t, 3H, *J*=6.2 Hz, CH_3); ^{13}C NMR δ 164.1, 69.8, 69.0, 62.7, 50.8, 37.3, 36.0, 34.3, 31.9, 29.6, 29.3, 29.1, 22.6, 16.4, 14.1.

Extractions of Am^{3+} and Eu^{3+} with CMP(O) tripodand-containing magnetical particles

An aqueous phase was prepared at varying HNO_3 concentrations (0.01-3M). Europium, as radioisotope ^{152}Eu, and americium, as radioisotope ^{241}Am, were added at an activity around 1500 kBq dm^{-3}, which corresponds approximatively to a concentration of 5×10^{-8}M for Am^{3+} and 1.5×10^{-9}M for Eu^{3+}. 10 mL of the aqueous phase was shaken with particles (300 mg) for 1 h and then separated by magnetic techniques. The initial and final concentrations of the lanthanides and actinides in the aqueous phases were determined using a single-channel γ analyzer with a NaI (Tl) well detector.

7.9 References

[1] (a) Horwitz, E. P.; Martin, K. A.; Diamond, H.; Kaplan, L. *Solvent Extr. Ion Exch.* **1986**, *4*, 449; (b) Horwitz, E. P.; Diamond, H.; Martin, K. A.; Chiarizia, R. *Solvent Extr. Ion Exch.* **1987**, *5*, 419.

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

[3] Matthews, S. E.; Saadioui, M.; Böhmer, V.; Barboso, S.; Arnaud-Neu, F.; Schwing-Weill, M. J.; Garcia Carrera, A.; Dozol, J. F. *J. Chem. Soc., Perkin Trans. 2* **1999**, 719.

[4] Boerrigter, H.; Verboom, W.; Reinhoudt, D. N. *J. Org. Chem.* **1997**, *62*, 7148.

[5] Arduini, A.; Böhmer, V.; Delmau, L.; Desreux, J.; Dozol, J.; Carrera, M. A. G.; Lambert, B.; Musigmann, C.; Pochini, A.; Shivanyuk, A.; Ugozzoli, F. *Chem. Eur. J.* **2000**, *6*, 2135.

[6] Peters, M. W.; Werner, E. J.; Scott, M. J. *Inorg. Chem.* **2002**, *41*, 1707.

[7] Pandey, A. K.; Gautam, M. M.; Shukla, J. P.; Iyer, R. H. *J. Membr. Sci.* **2001**, *190*, 9.

[8] Buchholz, B. A.; Tuazon, H. E.; Kaminski, M. D.; Aase, S. B.; Nuñez, L.; Vandergift, G. F. *Sep. Pur. Tech.* **1997**, *11*, 211.

[9] Naik, P. W.; Dhami, P. S.; Misra, S. K.; Jambunathan, U.; Mathur, J. N. *J. Radioanal. Nucl. Chem.* **2003**, *257*, 327.

[10] (a) Lebreton, S.; Newcombe, N.; Bradley, M. *Tetrahedron Lett.* **2002**, *43*, 2479; (b) Lebreton, S.; How, S. E.; Buchholz, M.; Yingyongnarongkul, B. E.; Bradley, M. *Tetrahedron* **2003**, *59*, 3945.

[11] Malinowska, E.; Górski, L.; Wojciechowska, D.; Reinoso-García, M. M.; Verboom, W.; Reinhoudt, D. N. *New J. Chem.* **2003**, *27*, 1440.

[12] (a) Mi, Y.; Bakker, E. *Anal. Chem.* **1999**, *71*, 5279; (b) Qin, Y.; Mi, Y.; Bakker, E. *Anal. Chim. Acta* **2000**, *421*, 207.

[13] Goldberg, I.; Meyerstain, D. *Anal. Chem.* **1980**, *52*, 2105.

[14] Moore, S. S.; Tarnowski, T. L.; Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc.* **1997**, *99*, 6398.

[15] Pearson, G. R. *J. Am. Chem. Soc.* **1963**, *85*, 353.

[16] Nuñez, L.; Buchholz, B. A.; Vandergift, G. F. *Sep. Sci. Tech.* **1995**, *30*, 1455.

[17] Kaminski, M.; Landsberger, S.; Nuñez, L.; Vandergift, G. F. *Sep. Sci. Tech.* **1997**, *32*, 115.

[18] Nuñez, L.; Kaminski, M. D. *J. Magn. Magn. Mater.* **1999**, *194*, 102.

[19] Matthews, S. E.; Parzuchowski, P.; Garcia-Carrera, A.; Grüttner, C.; Dozol, J. F.; Böhmer, V. *Chem. Commun.* **2001**, 417.

[20] Böhmer, V.; Dozol, J. F.; Grüttner, C.; Liger, K.; Matthews, S. E.; Rudershausen, S.; Saadioui, M.; Wang, P. *Org. Biomol. Chem.* **2004**, *2*, 2327.

[21] Haag, R. *Chem. Eur. J.* **2001**, *7*, 327.

[22] Grüttner, C.; Böhmer, V.; Casnati, A.; Dozol, J. F.; Reinhoudt, D. N.; Reinoso-García, M. M.; Rudershausen, S.; Teller, J.; Ungaro, R.; Verboom, W.; Wang, P. *J. Magn. Magn. Mater.* Accepted for publication.

[23] Meijler, M. M.; Arad-Yellin, R.; Cabantchik, Z. I.; Shanzer, A. *J. Am. Chem. Soc.* **2002**, *124*, 12666.

Summary

The work described in this Thesis deals with the synthesis of new cavitand- and tripodand-based ligands, their extraction properties, and their potentiometric response towards different cations, among them Am^{3+} and Eu^{3+}. A general introduction is given in Chapter 1. In addition, the contents of the Thesis are summarized.

Nuclear fission energy generation gives rise to highly radioactive waste due to the presence of plutonium and minor actinides. Chapter 2 deals with the different processes that are under investigation for the reduction of the highly radioactive waste. Special attention has been paid to the hydrochemical process (PUREX), which recovers uranium and plutonium. The different processes involved in the coextraction of actinides and lanthanides from the waste are reported. It is important, for the final conversion of the actinides into their short live isotopes, its separation from lanthanides. Therefore Chapter 2 also describes the selective extractants that are under investigation. In addition, an overview is given of known ligands that specifically bind actinides and/or lanthanides.

In Chapter 3 the preparation of different carbamoylmethylphosphonate (CMP), -phosphine oxide CMPO, and *N*-acyl(thio)urea-tetrafunctionalized cavitands is described. Liquid–liquid extractions were performed from aqueous nitric acid into dichloromethane or *o*-nitrophenyl hexyl ether (NPHE). The extraction of Am^{3+} and Eu^{3+} was studied in both the absence and presence of the hexabrominated cobalt bis(dicarbollide) anion (Br_6-COSAN) as a synergist. *N*-acyl(thio)urea cavitands are less effective extractants than the corresponding CMP(O) derivatives. However, they present an interesting selectivity for Am^{3+} over Eu^{3+} in the presence of Br_6-COSAN. Higher extraction efficiencies were achieved with the ionphores that have a propyl chain between the cavitand platform and the chelating groups.

Chapter 4 describes the results of the binding properties towards different cations of the CMP(O)- and *N*-acyl(thio)urea tetrafunctionalized cavitands as obtained from metal picrate extractions and the incorporation of the ionophores in ion selective electrodes (ISEs). Picrate extractions showed that there is more than a 40% increase of the Ag^{+}

extraction for *N*-acylthiourea cavitand derivatives in comparison with the single *N*-benzoyl-*N*'-benzylthiourea. This shows that the attachment of four *N*-acylthiourea moieties to a molecular platform improves the complexation behavior. The complexation behavior of cavitands functionalized with CMP(O) moieties or *N*-acyl(thio)urea moieties in ion selective electrodes was studied. The complex formation constants for these ionophores were obtained via potentiometric sandwich membrane measurements. CMP(O)-cavitands form very stable and stronger complexes than the *N*-acyl(thio)urea-tetrafunctionalized cavitands, which can be explained by the different nature of the chelating groups (CMP(O) *vs* *N*-acyl(thio)urea). The selectivity coefficients obtained with ion selective electrodes correlate well with the complex stability constants; CMP(O) cavitands are very selective for UO_2^{2+} and Pb^{2+} cations, whereas *N*-acyl(thio)urea cavitands have the highest selectivity for Ag^+. The correlation between the potentiometric selectivity and the ability of examined cavitands to form metal-ligand complexes is discussed.

Chapter 5 deals with the extraction properties for Am^{3+} and Eu^{3+} of appropriately functionalized cavitands substituted at the upper or lower rim with cobalt bis(dicarbollide) anions (COSAN). A comparative study showed that COSAN-containing cavitands functionalized at the upper rim with CMPO, *N*-acylthiourea, or picolinamide moieties have higher distribution coefficients than the corresponding reference cavitands, that do not contain COSAN. Two different spacers were used for the linkage of COSAN to the cavitand, an ethyleneglycol chain or a methyl spacer. It was found that long and flexible spacers result in an improvement of the extraction properties. COSAN-containing *N*-acylthiourea cavitand, which has a long and flexible spacer between the COSAN and the cavitand, has about 6000 times higher distribution coefficients than reference *N*-acylthiourea cavitand. Contrary to this result, COSAN-containing CMPO cavitand, which has a methoxy group as a spacer, has only 2 times higher distribution coefficients than the reference CMPO cavitand.

Chapter 6 deals with the synthesis, extraction and sensing behavior of trimethylolpropane-based tripodal ionophores with *N*-acyl(thio)urea and picolin(thio)amide as chelating units. The *N*-acylurea derivative has high separation factors at very low nitric acid concentrations for Am^{3+}/Eu^{3+} separation, although the distribution coefficients are low. In the presence of Br_6-COSAN as a synergist the distribution coefficients were increased considerably, especially in the case of the picolinamide derivative (>1000). It is also a very good ionophore for the extraction of Hg^{2+}, however, it forms so strong complexes that it cannot be used as ionophore in ion selective electrodes.

Chapter 7 deals with a study of two CMP(O) tripodands. All the techiniques employed in the other Chapters have been used in order to investigate the behavior of these ionophores towards different cations, paying special attention to Am^{3+} and Eu^{3+}. The last part of the chapter deals with solid-liquid extractions of Am^{3+} and Eu^{3+} performed with magnetica silica particles functionalized with CMP(O) tripodands. Particles with CMPO tripodand have about 10 times higher distribution coefficients than particles with CMP tripodand. The high distribution coefficients reached at low HNO_3 concentraction makes of the CMPO tripodand bearing particle a promising system for an industrial development.

Samenvatting

Het werk beschreven in dit proefschrift behandelt de synthese, extractie-eigenschappen en potentiometrische respons van nieuwe liganden. Deze op cavitanden gebaseerde en tripodand liganden zijn onderzocht op hun complexatiegedrag ten opzichte van verschillende kationen, waaronder Eu^{3+} en Am^{3+}. Hoofdstuk 1 begint met een algemene inleiding tot het onderwerp, gevolgd door een samenvatting van de inhoud van dit proefschrift.

Het opwekken van energie door middel van kernsplitsing leidt tot het ontstaan van hoog-radioactief afval vanwege de generatie van plutonium en hogere actiniden tijdens het splitsingsproces. In hoofdstuk 2 worden verschillende processen behandeld die onderzocht zijn met tot doel de hoeveelheid radioactief afval te verminderen. Speciale aandacht gaat hierbij uit naar het PUREX proces, dat de terugwinning van uranium en plutonium mogelijk maakt. Verschillende processen die in gebruik zijn voor de gezamenlijke extractie van actiniden en lanthaniden uit nucleair afval worden behandeld. Voor de uiteindelijke omzetting van actinide in kort levende isotopen is het van wezenlijk belang dat de actiniden gescheiden worden van lanthaniden. Dit is de reden dat in hoofdstuk 2 tevens een beschrijving wordt gegeven van processen die een selectieve scheiding kunnen bewerkstelligen. Tot slot wordt een overzicht gegeven van liganden die specifiek actiniden en/of lanthaniden kunnen complexeren.

In hoofdstuk 3 wordt de synthese van verschillende carbamoylmethylfosfonaat (CMP), -fosfienoxides (CMPO) en *N*-acyl(thio)ureum tetragefunctionaliseerde cavitanden beschreven. Vloeistof/vloeistof extracties van ionen werden uitgevoerd vanuit verdund salpeterzuur naar dichloormethaan en *o*-nitrophenylhexylether (NPHE). De extractie van Am^{3+} en Eu^{3+} werd bestudeerd in aan- en afwezigheid van het hexa-gebromineerde cobalt bis(dicarbollide) anion (Br_6-COSAN) als synergent. Extracties met *N*-acyl(thio)ureum cavitanden zijn minder effectief als de overeenkomstige CMP(O) derivaten. Een interessant gegeven is echter de selectiviteit van deze *N*-acyl(thio)ureum cavitanden voor de binding van Am^{3+} ten opzichte van Eu^{3+} in de aanwezigheid van Br_6-COSAN. Hogere extractieefficiënties werden behaald met ionoforen die een propylketen tussen de cavitand en de chelerende groepen hebben.

In hoofdstuk 4 worden de bindingseigenschappen beschreven van CMP(O) en *N*-acylthioureum tetragefunctionaliseerde cavitanden t.a.v. verschillende kationen op grond van picraatextracties. Tevens wordt het gebruik van deze ionoforen in ion selective electrodes beschreven. Picraatextracties laten zien dat er een toename van meer dan 40% is voor de extractie van Ag^+ met *N*-acylthioureum cavitanden ten opzichte van *N*-benzoyl-*N*'-benzylthioureum. Het complexatiegedrag van cavitanden, gefunctionaliseerd met CMP(O) of *N*-acylthioureumgroepen, in ion selectieve electrodes werd bestudeerd. Uit deze resultaten blijkt dat door vier *N*-acylthioureumgroepen aan een platform te verbinden, het complexatiegedrag aanmerkelijk wordt verbeterd. Complex vormingsconstantes van deze ionoforen werden verkregen via potentiometrische sandwich membraanmetingen. CMP(O)-cavitanden vormen erg stabiele, en sterkere complexen dan de *N*-acyl(thio)ureum gefunctionaliseerde cavitanden, hetgeen valt te verklaren uit het verschil in coördinerende groep [CMP(O) en *N*-acylthioureum]. De selectiviteitsconstanten verkregen m.b.v. ionselectieve electrodes en de complexstabiliteitsconstanten vertonen een grote mate van correlatie; CMP(O) cavitanden vertonen een grote selectiviteit voor UO_2^{2+} en Pb^{2+} kationen, terwijl *N*-acylthioureum cavitanden een hogere selectiviteit hebben voor Ag^+. De correlatie tussen de potentiometrische selectiviteit en het vermogen van de onderzochte cavitanden om metaalionen te complexeren wordt besproken.

In hoofdstuk 5 worden de extractie-eigenschappen beschreven van gefunctionaliseerde cavitanden bedoeld voor selectieve scheiding van Am^{3+} en Eu^{3+}. Behalve dat deze cavitanden zijn voorzien van diverse chelerende groepen, CMPO, *N*-acylthioureum en picolinamide, is de onder- dan wel bovenkant gefunctionaliseerd met cobalt bis(dicarbollide) anionen (COSAN). Het blijkt dat cavitanden gefunctionaliseerd met een chelerende groep aan de bovenkant en een COSAN aan de onderkant, veel hogere distributiecoëfficiënten hebben dan vergelijkbare cavitanden zonder COSAN functionaliteit. Twee spacers van verschillende lengte, een ethyleenglycol en een methyleenspacer, werden gebruikt om het COSAN met de cavitand te verbinden. Uit experimenten bleek dat gebruik van een lange en flexibele spacer resulteerde in een verbetering van de extractie-eigenschappen. De cavitand, gefunctionaliseerd met een *N*-acylthioureum en een via een lange, flexibele spacer verbonden COSAN, bleek een distributiecoëfficiënt te hebben die ongeveer 6000 maal hoger is dan een overeemkomstig cavitand zonder COSAN. Echter, een CMPO gefunctionaliseerd cavitand met daaraan een COSAN verbonden via een methoxygroep heeft een distributiecoëfficiënt die slechts twee maal hoger is dan een vergelijkbaar CMPO gefunctionaliseerd cavitand.

De synthese, extractie-eigenschappen en gedrag als sensor van op trimethylolpropaan gebaseerde tripodand ionoforen met *N*-acylthioureum en picolin(thio)amide als coördinerende groepen worden in hoofdstuk 6 beschreven. De ionofoor met *N*-acylureum groepen heeft bij een erg lage salpeterzuurconcentratie hoge scheiding factoren voor de scheiding van Am^{3+} en Eu^{3+}, echter de distributiecoëfficiënt is laag. In aanwezigheid van Br_6-COSAN als synergent zijn de distributiecoëfficiënten aanmerkelijk hoger, in het bijzonder in geval van de picolinamide verbinding (>1000). Deze verbinding is tevens een zeer goede ionofoor voor de extractie van Hg^{2+}. Er vindt echter dermate sterke complexatie plaats dat deze verbinding niet als ionofoor gebruikt kan worden in ionselectieve electrodes.

Hoofdstuk 7 beschrijft het extractiegedrag van twee CMP(O)-gefunctionaliseerde tripodand ionoforen, waarbij in het bijzonder aandacht werd besteed aan de extractie van Am^{3+} en Eu^{3+} ionen. Het laatste deel van het hoofdstuk behandelt vaste stof – vloeistof extracties van Am^{3+} en Eu^{3+}, uitgevoerd met magnetische silicadeeltjes gefunctionaliseerd met CMP(O) bevattende drie-armige liganden. Deeltjes met CMPO-tripodand hebben een distributiecoëfficiënt die ongeveer 10 maal zo hoog ligt dan deeltjes gefunctionaliseerd met CMP-tripodand. De hoge distributiecoëfficiënten die worden bereikt bij een lage concentratie HNO_3 maakt van het silicadeeltje gefunctionaliseerd met CMPO-tripodand een veelbelovend systeem voor industriële toepassingen.

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Marta

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