SYNTHESIS OF THE C$_3$-SYMMETRIC TRIPHENOXYMETHANE BASED LIGANDS
AND EVALUATION OF THEIR EXTRACTION BEHAVIOR
WITH LANTHANIDE METAL IONS

By

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To my Travis, and all my family members
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SYNTHESIS OF THE C$_3$-SYMMETRIC TRIPHENOXYMETHANE BASED LIGANDS AND EVALUATION OF THEIR EXTRACTION BEHAVIOR WITH LANTHANIDE METAL IONS

By

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Major: Chemistry

The reprocessing of highly radioactive nuclear waste is complex due to close similarities in chemical and physical properties of Ln(III) and An(III) and is only possible when these elements are separated. The C$_3$-symmetric DPA functionalized triphenoxymethane platform has been offered as a chelate for An(III)/Ln(III) separation. Thio-DPA functionalized triphenoxymethane platform has also been prepared along with the N-oxide preorganized ligand. The potency of ligands was examined with a series of eleven lanthanides using liquid-liquid extraction. The influence of chelate properties was studied through variation of substituents on the platform and on the binding arm; the influence of the diluent and COSAN was also examined. The efficiency of chelates was determined by UV-vis spectroscopy. Purity of compounds was confirmed by NMR spectroscopy, mass spectrometry and elemental analysis. Results showed that DPA functionalized triphenoxymethane platform has moderate extraction ability towards lanthanides. The addition of the counterion COSAN significantly improves percent extraction, but the change of solvent from DCM to more non-polar 1-octanol reduces it to zero. The poor solubility of the chelate explains these results: under standard
conditions (DCM as a solvent) the ligand is a weak extractant; the addition of the counterion COSAN helps solubilize the extracted complex, facilitating the extraction and resulting in elevated extractability; the solubility of the ligand in 1-octanol is very low resulting in no extractability at all. The extraction ability of the thio-derivative was lower than the oxygen bearing DPA chelate due to more covalent character of the sulfur donor atoms. The tripodal N-oxide ligand showed very poor extractability, even with the COSAN synergist. The problem of An(III)/Ln(III) separations still remains unresolved and further investigations in this area are necessary.
CHAPTER 1
INTRODUCTION

Currently, nuclear power generates 15% of the total world’s electricity from 441 nuclear reactors, but the International Energy Outlook projects an increase in nuclear electricity consumption by 1000 billion kWh by 2030. Expansion in the use of nuclear power would significantly reduce the greenhouse gas emissions such as CO$_2$, SO$_2$ and NO$_x$, generated from combustion of fossil fuels (coal, oil and natural gas): to generate the same amount of electricity, a nuclear reactor requires 60 times less uranium ore compared to the amount of coal needed for a coal fired power plant. Given the increasing prices fossil fuels, nuclear power seems economically and environmentally reasonable solution. Moreover, nuclear energy could be used to produce large quantities of hydrogen gas, potentially a major energy source.$^1$

Despite all the advantages, the number of operating nuclear reactors has been declining since Chernobyl accident in 1986, and until now nuclear programs are suppressed due to fears of weapon proliferation and radioactivity hazards. Most radioactivity of the nuclear waste comes from transuranium actinides; in addition to actinides, retired fuel rods contain depleted uranium $^{238}$U, uranium $^{235}$U and small amount of fission products. Spent nuclear fuel can be managed in several ways: 1) direct geologic disposal; 2) long term surface or near-surface storage; and 3) reprocessing. The amount of high level waste (HLW) worldwide is currently increasing by about 12,000 metric tons every year, and it accounts for over 95% of the total radioactivity produced in the process of nuclear electricity generation.$^2$
Nuclear Fuel Reprocessing

Research into spent fuel reprocessing has made some progress over the past few decades. It was discovered that transmutation can drastically reduce radioactivity and decrease half-life of the long-lived actinides. Unfortunately, transmutation is inhibited by the presence of even small amounts of lanthanides due to their high neutron absorption cross section; therefore, the separation of actinides from lanthanides is the foremost issue in the waste reprocessing.

Chemistry of Actinides and Lanthanides

The partitioning of Ln(III) from Th(IV), U(VI), Pu(IV), Np(V) can be achieved by exploiting the higher oxidation states of the latter elements, but the separation of trivalent actinides from trivalent lanthanides remains a challenge because of the similarities in their chemical and physical properties. Both groups of elements are classified as hard Lewis acids. They have the same ionic radii, the same oxidation state (3+) and their most common coordination number is nine. The similarity in the ionic radii is due to lanthanide and actinide contraction where the ionic radius decreases with the increasing atomic number. The inability of the relatively small spatial extension of the 4f and 5f orbitals to compensate for the steadily increasing nuclear charge causes radii to contract. For lanthanides, the contraction is approximately 20%, e.g. for CN = 9, \( r(\text{La}^{3+}) = 1.216 \, \text{Å} \) and \( r(\text{Yb}^{3+}) = 1.075 \, \text{Å} \). Because of the difference in ionic radii the intra-group separation is easier to accomplish then inter-group separation.

The only major difference between 5f and 4f elements is a more covalent contribution of the 5f actinides to the ionic bonding. The 5f, 6d, 7s and 7p orbitals have similar spatial extensions which promote a direct overlap with the orbitals of suitable ligands. Lanthanides do not demonstrate such behavior, suggesting that a more
covalent bonding in case of actinides can be exploited for actinide and lanthanide partitioning.

An enhanced covalent character of transuranium elements was first described by Diamond et al. who noticed that in high concentrations of hydrochloric acid, actinides are elute faster than lanthanides. The elution rates of actinides (americium and curium) increase with increasing acid concentration, while the elution rates of lanthanides decreased. An actinide/lanthanide separation factor (SF) of 10 have been reported with 6-12 M hydrochloric acid. It was postulated that actinides can form complexes with chloride ions to a greater extent than with lanthanides. Although the enthalpy of the complex formation did not confirm the covalent nature of the actinide binding, the experimental data proved that the most successful separations were achieved with extractants that provide better covalent interactions.

**Separation of An(III) from Ln(III)**

The most effective methods for An/Ln separations are ion exchange and solvent extraction. Both involve the transfer of the charged metal ion from an aqueous phase to an immiscible organic phase with subsequent charge neutralization. The principal difference between these two methods is the solvating properties of the extracted complex. The transfer of the metal cation from the aqueous to the organic phase occurs in several steps. First, the cation must become less hydrophilic by partial or full dehydration at the interfacial zone. Then, the transfer is accompanied with the rearrangement of the solvent in order to stabilize the new extracted complex. The efficiency of the separation is measured by the ability of the extractant to accomplish phase transfer. The energetic requirement for a 99% separation, which corresponds to the separation factor (SF) of 100, is 11.4 kJ/mol (2.7 kcal/mol). It is comparable to the
energy of a hydrogen bond and accounts for approximately 1.5% of the total free energy of hydration of lanthanides which is 650-750 kJ/mol. The synergistic effect can be attained when several extractants are used in combination. For example, a solvating extractant will enhance the dehydration, while a chelating extractant will facilitate the ion transfer into the organic phase. If the synergist is highly hydrophobic, it can act as a surfactant like the chlorinated cobalt bis(dicarbollide), COSAN. According to the molecular dynamic study, COSAN concentrates on the organic side of the interface. Hydrophilic cations, which are generally "repelled" by the aqueous interfaces, are attracted by the COSAN, promoting the transfer of metal ions into the organic phase.

**Extractants for An(III) and Ln(III) Separation**

So far, the most important industrial extractant for the removal of tetra- and hexavalent actinides from other fission products is tributyl phosphate (TBP, Figure 1-1) which is utilized in PUREX (Plutonium URanium Extraction) process. One contact with 30% TBP in dodecane removes 99% of uranium and most of the plutonium, but unfortunately TBP cannot separate trivalent americium, curium and pentavalent neptunium from other fission products, so TRUEX (Trans Uranium EXtraction) process has to be employed. The TRUEX process uses a mixture of 0.2 M carbamoylmethylphosphine oxide (CMPO) (Figure 1-1) and 1.2 M TBP in n-dodecane. A TRUEX extraction system shows good selectivity of tri-, tetra- and hexavalent actinides over most of the fission products, but the key problem of actinide/lanthanide separation is still not accomplished.
Figure 1-1. Structure of chelates for An/Ln separation: a) Tri-n-butyl phosphate (TBP); b) carbamoylmethylphosphine oxide (CMPO); c) diisodecylphosphoric acid (DIDPA); d) bridge-substituted tetraalkylmalonamide; e) bis(triazinyl) pyridines (BTP); Cyanex 301.

Another type of organophosphorus extractant, diisodecylphosphoric acid (DIDPA, Figure 1-1), is used for the separation of transuranium elements from lanthanides. Very high extraction of actinides was shown by the mixture of 0.5 M DIDPA and 0.1 M TBP in dodecane. But the DIDPA extractant is also unable to separate trivalent actinides from trivalent lanthanides. In addition, organophosphorus extractants are not fully incinerable, which creates a problem with secondary waste generation.

French researchers came up with an idea of diamide extractants (DIAMEX process), which follow the CHON principle. Extractants containing only C, H, N, and O elements are fully incinerable at the end of the processing, thus, allow for a reduction in secondary waste. Malonamides, with general formula presented in Figure 1-1, dissolve in dodecane and give distribution ratios \((D)\) for Am(III) of approximately 10 at 3 M HNO\(_3\). Investigations with diglycolamides (DGAs), used showed that these are the
most efficient chelates among diamides. They coordinate to the metal through two
carboxylic and one ether oxygen.\textsuperscript{10} It was noted that central oxygen adopts capping
position in a tricapped trigonal prismatic (TTP) geometry.\textsuperscript{10,11} DGAs are successful in
extracting An(III), (IV) and (V),\textsuperscript{10} but they are less efficient in extracting lighter
lanthanides compared to heavier ones, in particular La(III).\textsuperscript{11,12}

By far, the most efficient lanthanide/actinide separation process is the SANEX
(Selective ActiNide EXtraction process) which uses nitrogen bis(triazinyl) pyridines\textsuperscript{13-15}
BTPs, and sulfur Cyanex\textsuperscript{16-18} (Figure 1-1) containing extractants. Very high separation
factors (SF) were achieved with these ligands; however, radiation stability and
degradation occurring upon contact with concentrated acids are of a great concern.\textsuperscript{2}

BTPs are one of the most effective ligands in actinide and lanthanide separations,
with $SF_{\text{Am/Eu}}$ greater that 100 known for liquid-liquid extractions. Theoretical
investigations, performed to elucidate the selectivity of BTPs towards actinides, showed
that the cavity formed by nitrogen atoms of the BTP ligand is too small to accommodate
lanthanides. In addition, calculated positive atomic charge on the central ring repels
Ln(III),\textsuperscript{13} which agrees with the structural studies of Ln-BTP complexes. Geist \textit{et al.} also
reported that higher affinity of the ligand for An(III) is associated with a higher
thermodynamic stability of the actinide-BTP complex.\textsuperscript{15}

The commercial extractant Cyanex 301, bis(2,4,4-trimethylpentyl)dithiophosphinic
acid (Figure 1-1), when purified and used for the partitioning of Am(III) from Eu(III) gives
a SF of 5900 in favor of Am(III). The significant drawback of this extractant is that the
separation can only be achieved when the acidity is lowered from 1 M to 0.04 M HNO$_3$. 

The dilution is highly undesirable due to the large increase in the amount of generated waste.\textsuperscript{2}

**Optimization of Ligands for An(III) and Ln(III) Extraction**

Lanthanides and actinides exist in solution as highly hydrated metal ions, thus complexation by bi- or tridentate ligands may be energetically unfavorable due to increasing enthalpy of dehydration and only slight compensation by increasing entropy.\textsuperscript{18} To decrease the net energy of complexation and increase the strength of entropic effect, multidentate ligands can be attached to a platform base.

Significant improvement in extractability has been observed when preorganizing a ligand on a calix[4]arene\textsuperscript{19-22} or a triphenoxymethane platform\textsuperscript{8,23,24} (Figure 1-2). Scaffolds became attractive for preorganization due to the ease of synthesis and the ability to attach the chelating ligand at the lower and at the upper rim of the platform.

![Figure 1-2. Structure of calix[4]arene and triphenoxymethane platform: a) calix[4]arene; b) triphenoxymethane platform.](image_url)

Preorganization has other benefits, for example, the solubility and flexibility of the ligand can be easily altered through modifications of the substituents in the ortho and para positions of the platform relative to the phenolic oxygen atoms. Bulky groups such as tert-pentyl increase the solubility in non-polar solvents such as 1-octanol, which is beneficial from the environmental point of view. They can also restrict the flexibility of the ligand which may result in decreased extraction efficiency. Flexibility can have a big
effect on the extraction strength of a ligand. For example, when a more flexible tris-CMPO derivative was prepared with a three carbon linker between the platform and the CMPO moiety, the extraction strength increased by more than 100%. Besides substituents on the tripodal base and the length of a carbon linker, substituents on the binding arm can also have an effect on the extraction performance due to steric and electronic effects. It means that the substituents for the triphenoxymethane platform and chelating arm have to be chosen very carefully for the optimization of the solubility and flexibility of the ligand.

The work on calixarenes began in the early 90s when Hozwitz et al. studied the Am-CMPO complex formed in the TRUEX process after extraction. It was discovered that three CMPO molecules bind Am(III) in a bidentate fashion, three NO$_3^-$ counterions balance positive charge of Am(III) and one HNO$_3$ molecule forms hydrogen bonds with carboxylic oxygen of the CMPO ligand (Figure 1-3). It led to the idea of a platform which can accommodate three or four CMPO groups, changing the stoichiometry, composition and steric requirements of the extracted species.$^{19}$ Preorganization of this type allows

![Figure 1-3. Possible solution structure (schematic) of the americium(III) nitrato-CMPO complex at high HNO$_3$, concentration.$^{25}$]
optimization of the coordination geometry of the CMPO moieties, and ultimately results in a better extraction and selectivity properties.

One of the most recent studies with calixarenes involves calix[4]arene functionalized with four CMPO molecules on the upper rim. Extractions performed in 1M HNO$_3$ in dichloromethane reveal that the best separation factor between Th(IV)/Eu(III) is achieved with a ligand which has a three carbon spacer between the platform and the CMPO group. The ligand with a four carbon spacer has highest percent extraction for tetravalent thorium (>90%), but it also has high percent extraction for lanthanides; La(III), Eu(III) and Yb(III) were extracted in 70, 68 and 37%, respectively.$^9$ Good extractability of lanthanides is highly undesirable because it decreases the An(III)/Ln(III) separation factor.

The problem of high %E of Ln(III) is eliminated when a CMPO molecule is attached to a closely resembling triphenoxyxymethane platform (tris-CMPO). It still demonstrates high %E for Th(IV) but has very low and consistent %E for Ln(III). With tris-CMPO, Th(IV) is almost completely extracted from 1 M HNO$_3$ using 10 equivalents.

![Figure 1-4. CMPO functionalized triphenoxyxymethane platform: a) triphenylmethane platform with CMPO functions at the upper and at the lower side.](http://example.com/f14.png)
of the ligand, while under the same conditions only 2% of Th(IV) is extracted by CMPO ligand without a platform (mono-CMPO) when 30 equivalents of the ligand is used. It can be concluded that preorganization on the triphenoxymethane platform increases the affinity of a metal towards the ligand binding site due to the fact that three arms, precisely arranged on a platform, provide an optimal coordination environment for the metal. Solid state studies with Ln(III) and Th(IV) tris-CMPO showed similar sizes, shapes and charges for these complexes, which means that the selectivity for Th(IV) is probably due to higher intrinsic stability of Th(IV) tris-CMPO complex and not to the structural differences between the complexes.\textsuperscript{8,15,24} Inspired by this work, Rudzevich at al. developed two tripodal ligands where CMPO group was attached to the lower rim of the triphenoxymethane scaffold (Figure 1-4). Over the range of nitric acid concentrations (up to 5 M) both ligands extract Am(III), on average, two times better than Eu(III).\textsuperscript{26}

Another attempt to utilize the advantages of triphenoxymethane platform and the preferential binding of actinides to soft donor atoms was exercised in the development of a chiral tris(2-pyridylmethyl)amine ligands (Figure 1-5). Encouraged by the work performed by Wietzke \textit{et al.}, who reported a $SF_{\text{Am/Eu}}$ of 10 for tris[(2-pyrazinyl)methyl] amine (tpza) ligand,\textsuperscript{27} the authors prepared three tridentate pyridine podands: $R$-tris-(pyridylmethyl)amine, $R,R$-tris(pyridyldimethyl)amine, $R,S$-tris(pyridyldimethyl)amine (Figure 1-5), which have chirality on the methylene group of the terminal pyridyl. The highest separation factor ($SF \approx 25$) was observed at pH = 4.76 for the $R,S$-tris(pyridyl-dimethyl)amine derivative with 2-bromodecanoic acid which was used as a counter ion.
The authors explain that the stereochemical substitution provides favorable coordination of Am(III) over Eu(III).²⁸

Figure 1-5. Structure of pyridine podants: a) tris[(2-pyrazinyl)methyl]amine (tpza); Structures of chiral tripod ligands: b) R-tris(pyridylmethyl)amine; c) R,R-tris(pyridyldimethyl)amine; d) R,S-tris(pyridyldimethyl)amine.

**Research Objectives**

In view of growing environmental concerns and accumulation of the high level nuclear waste, it is imperative to develop new techniques that will allow reducing, or completely eliminating hazards from radioactive waste. Separation of actinides from lanthanides not only decreases the amount of harmful waste but also provides the opportunity to convert these harmful elements into relatively innocuous lead. Current research is focused on developing organic molecules that are capable of binding 4f and 5f elements. The ultimate goal is to prepare chelates that will preferentially bind 5f elements and will be able to remove them from high level raffinate. The binding ability of our chelates was tested using eleven lanthanides; and while extraction of Ln(III) is not the goal of industrial separation, tests with rare earth elements can predict how the ligand will behave with transuranium elements.
CHAPTER 2
PYRIDINE-2,6-DICARBOXAMIDE BASED EXTRACTANTS AND THEIR ABILITY TO REMOVE 4F ELEMENTS FROM 1 M NITRIC ACID

Introduction

So far, the most effective way for An(III)/Ln(III) partitioning is a liquid-liquid extraction. Most common extractants are carbamoylmethylphosphine oxide (CMPO)\textsuperscript{9,29}, diglycolamides (DGAs)\textsuperscript{12,30}, bis(triazinyl) pyridines (BTPs)\textsuperscript{13-15}, and Cyanex\textsuperscript{16-18}. These ligands were used as either single molecules or preorganized chelates. We report the results of liquid-liquid extractions of dipicolinamides (DPAs)\textsuperscript{31,32} ligands which were preorganized on a triphenoxymethane platform.

DPAs have already been evaluated as extractants for An(III)/Ln(III) separation. One of the advantages of picolinamides is that they are completely incinerable. Also, unlike other extractants they have hard (oxygen) and soft (nitrogen) donor atoms, which are available for metal binding. It was shown that soft donor ligands have higher affinity for An(III).\textsuperscript{3,33} Thus, the combination of hard and soft properties is interesting for An(III)/Ln(III) separation.\textsuperscript{33}

Early studies report the Am(III)/Eu(III) separation factor ($SF_{Am/Eu}$) of 1.4; extractions were performed with $N,N$-dimethyl-$N,N$- dibutyl-2,6-dicarboxamide in benzonitrile.\textsuperscript{33} Extractions with $N^2,N^2,N^6,N^6$-tetrahexylypyridine-2,6-dicarboxamide and

![Figure 2-1. Structure of dipicolinamide (DPA) derivatives: a) $N,N$-dimethyl-$N,N$- diphenylypyridine-2,6-dicarboxamide; b) $N,N$-diethyl-$N,N$-di(p-tolyl)pyridine-2,6-dicarboxamide.](image)
\[N^2,N^2,N^6,N^6\text{-tetra(2-ethylhexyl)pyridine-2,6-dicarboxamide}\] in different solvents, such as benzene, toluene, cyclohexane, chloroform, carbon tetrachloride and n-decane show that aromatic solvents give the highest distribution values \((D)\). Chloroform gives the lowest \(D\) values, probably due to hydrogen bonding between CHCl\(_3\) and the ligand.\(^{34}\)

The extraction ability of DPAs depends on the nature of substituents on the amide groups;\(^{32,33}\) for example, extractions from nitric acid solutions with pyridine-2,6-dicarboxamide in chloroform show that \(N,N\text{-diethyl-}\text{-}N,N\text{-di(p-tolyl)pyridine-2,6-dicarboxamide}\) extract Am(III) better than \(N,N\text{-dimethyl-}\text{-}N,N\text{-diphenylpyridine-2,6-dicarboxamide}\) \(D_{Am} = 11\) and \(D_{Am} < 0.25\) respectively (Figure 2-1). Results also showed that \(D\) values increase considerably when HClO\(_4\) is used instead of HNO\(_3\); the same ligands give \(D_{Am} = 37\) and \(D_{Am} = 1.6\) respectively.\(^{32}\)

Extraction efficiency also depends on acid concentration. Generally, percent extraction \((\%E)\) increases with increasing \([H^+]\): \(D_{Eu}\) increases from \(3 \times 10^{-4}\) to 1.6 when going from 1 M to 5 M HNO\(_3\) in the extraction with \(N,N\text{-dimethyl-}\text{-}N,N\text{-diphenylpyridine-2,6-dicarboxamide}\).\(^{31}\) The same tendency is observed in perchloric acid: \(D_{Eu}\) of 0.61 and \(D_{Eu}\) over 103 for 0.5 M and 6 M HClO\(_4\) respectively with \(N,N,N,N\text{-tetrabutylpyridine-2,6-dicarboxamide}\).\(^{32}\) Shimada \textit{et al.} explains that with acid concentrations greater than 3 M, it participates in extraction of Ln(III).\(^{31}\)

Dipicolinamides are weak extractants when acid concentration is lower than 2 M. However, the presence of chlorinated cobalt dicarbollide (COSAN) significantly increases \(\%E\). Results, presented by Peterman \textit{et al.} indicate that \(N,N,N,N\text{-tetrabutylpyridine-2,6-dicarboxamide}\) is the most promising chelate. The highest \(D\) ratios \((D_{Eu} \text{ and } D_{Am} \text{ more than } 3000)\) were observed with 0.03 M ligand at 1 M HNO\(_3\), 0.13 M
COSAN and 0.027 M PEG-400 in phenyl trifluoromethylsulfone (FS-13).\textsuperscript{36} In the absence of PEG-400, the same ligand showed $D_{Am} = 20$ with 0.06 M COSAN in m-nitrobenzofluoride (F-3).\textsuperscript{36}

**Results and Discussion**

**Ligand Design**

The following report presents the synthesis and evaluation of the new ligands where three DPA molecules, 6-(diethylcarbamoyl)picolinic acid, \((4)\) or 6-(diisopropylcarbamoyl)picolinic acid \((5)\) were tethered through phenol oxygens or amine nitrogen to the upper or to the lower side of the platform, using peptide coupling reagent PyBOP (Figure 2-2). All ligands were fully characterized and their ability to extract Ln(III) ions from 1 M nitric acid was investigated. The effect of the solvent was analyzed by changing the composition of the organic phase. The extractions were performed in DCM and in 1-octanol. In addition, the extraction experiments with one ligand were performed

![Figure 2-2. Structure of PyBOP and COSAN: a) benzotriazole-1-yl-oxy-trispyrrolidinophosphonium hexafluorophosphate (PyBOP); b) cesium (8,9,12,8',9',12'-hexachloro-1,2-dicarbollide)cobaltate (COSAN)](image-url)
in the presence of the COSAN counterion (Figure 2-2), and the results of this experiment were compared to the structurally similar preorganized chelate which was studied earlier by the former member in our group.\textsuperscript{37}

Since phenolic oxygens are oriented in “all up” conformation,\textsuperscript{23} it is convenient to tether various moieties onto the platform. Depending on the type of a platform, these moieties can be attached to the upper or to the lower side of the scaffold. The synthesis of the three $C_3$-symmetric platforms $2\text{-}2$, $3\text{-}2$ and $1\text{-}6$, where $2\text{-}2$ and $3\text{-}2$ can be preorganized on the upper side and $1\text{-}6$ at the lower side is shown in Schemes 2-1, 2-2 and 2-3.

![Scheme 2-1](image_url)

**Scheme 2-1.** Synthesis of the triphenoxy methane platform with two CH$_2$ carbon linker.

a) $K_2$CO$_3$, NaI, chloroacetonitrile, acetone; b) LAH, DCM.

Since flexibility of the ligand has a large impact on the extraction performance, platform $3\text{-}2$ (Scheme 2-2) was prepared as a more flexible derivative of the upper side functionalized platform compared to $2\text{-}2$ (Scheme 2-1). The structural difference between these molecules is the length of a carbon spacer (-CH$_2$-), which is two in case...
Scheme 2-2. Synthesis of the triphenoxymethane platform with three CH$_2$ carbon linker.

a) Cs$_2$CO$_3$, N-(3-bromopropyl)phthalimide, DMF; b) N$_2$H$_4$, EtOH.

of 2-2 and three in case of 3-2. The ligands 2-2-4 and 3-2-4 were prepared by coupling
6-(diethylcarbamoyl)picolinic acid (4) to the tripodal bases 2-2 and 3-2, respectively,
using PyBOP (benzotriazole-1-yl-oxy-trispyridinophosphonium hexafluoro-phosphate)
reagent (Scheme 2-3).

Scheme 2-3. Synthesis of tris-DPA ligands 2-2-4 and 3-2-4: PyBOP, DMF,
diisopropylethylamide.
The platform 1-6 was prepared according to the Scheme 2-4. The ligands 1-6-4 and 1-6-5 were synthesized by attaching the 6-(diethylcarbamoyl)picolinic acid (4) or 6-(diisopropyl-carbamoyl)picolinic acid (5) to the lower side of the platform 1-6 (Scheme 2-6). Tripodal chelates 1-6-4 and 1-6-5 were synthesized to investigate the influence of the substituents on the chelating arm (4 or 5). The compound 1-6-5 has a slightly more bulky isopropyl group attached to the terminal amine instead of ethyl group (1-6-4). The effect of these substituents is important to explore since, a more bulky isopropyl group will increase the solubility of the ligand in the organic phase and increase the electron density on the nitrogen atom due to +M effect, increasing the covalent character of the DPA group. On the other hand, steric effects may prevent the metal from efficient binding to the nanodentate chelate, resulting in decreased extraction efficiency.

In order to evaluate the dependence of the extractability on the substituents of the platform base itself, ligand 1-6-4 was compared to the previously reported ligand 0-6-4. The structural difference between 0-6-4 and 1-6-4 is the substituent in the ortho position relative to the methoxy group, where R = H in case of 0-6-4 and R = Me in case of 1-6-
4. The methyl derivative (1-6-4) is expected to be more soluble in the organic phase, and thus should have better extraction performance.

\[
\text{Scheme 2-5. Synthesis of the triphenoxymethane platform 0-6. a) Mel, K}_2\text{CO}_3, \text{DMF}; \text{b) Zn, CaCl}_2\cdot2\text{H}_2\text{O, EtOH.}
\]

The platform 0-6\textsuperscript{37} and the ligand 0-6-4\textsuperscript{37} were prepared by the former member in our group, Dr. Ozge Ozbek. Ligand synthesis utilized the same coupling reaction with the PyBOP reagent, where 6-(diethylcarbamoyl)picolinic acid (4) was attached to the platform 0-6 (Scheme 2-6). The synthetic route for 0-6 (Scheme 2-5) appeared to be less efficient than the route for the preparation of compound 1-6. In the latter case, the condensation of the tripodal base 1-3 was followed by the protection of the phenolic oxygen (1-4) and nitration (1-5); while in the case of 0-6, the nitration step (0-4) preceded protection of the

\[
\text{Scheme 2-6. Synthesis of tris-DPA ligands 0-6-4, 1-6-4 and 1-6-5. Pybop, DMF, diisopropylethylamide.}
\]
phenolic oxygen (0-5). The modification of the synthetic procedure resulted in the increase of the overall yield from 50% for 0-6\textsuperscript{37}, to 76% for 1-6.

The 6-(diethylcarbamoyl)picolinic acid (4) was prepared according to the procedure reported by Johansen\textsuperscript{38} and Elhabiri.\textsuperscript{39} The derivative of 4, 6-(diisopropylcarbamoyl)picolinic acid (5), was prepared according to modified procedure for 4\textsuperscript{37} (Scheme 2-7). All ligands presented in this study were prepared in good yields and purity and have been characterized by \textsuperscript{1}H and \textsuperscript{13}C NMR spectroscopy.

\[
\begin{align*}
\text{HO-} & \quad \text{HO-} \\
\text{N} & \quad \text{N} \\
\text{COOH} & \quad \text{COCH}_3 \\
\text{(a)} & \quad \text{(b)} \\
\text{HO-} & \quad \text{HO-} \\
\text{N} & \quad \text{N} \\
\text{COCH}_3 & \quad \text{Cl} \\
\text{(c)} & \quad \text{(5)}
\end{align*}
\]

Scheme 2-7. Synthesis of the DPA groups 4 and 5. a) MeOH, H\textsubscript{2}SO\textsubscript{4}, reflux 15 min, stir for 10 hrs; b) SOCl\textsubscript{2}, DCM, reflux; c) DCM, HNEt\textsubscript{2}, reflux; KOH, HCl.

**Evaluation of Extraction Performance**

The extraction ability was studied with the series of eleven lanthanides. In addition, the extractability of 1-6-4 was tested in the presence of chlorinated cobalt dicarbollide (COSAN) counterion and compared to the behavior of 0-6-4 under the same conditions.

The results of extraction experiments with 2-2-4 and 3-2-4 demonstrated that both ligands have moderate ability to remove lanthanides from 1 M HNO\textsubscript{3} (Figure 2-3). Ligand 3-2-4 has showed slightly higher %E and D values; however, the increase was not as high as anticipated, and taking into consideration the percent error, can be
considered insignificant (Table 2-1). Apparently, the length of the carbon spacer on the upper side preorganized triphenoxymethane based chelate does not influence the extraction performance of the ligand.

Figure 2-3. Metal extraction percentages ($\%E$) for ligands 2-2-4 and 3-2-4 using $10^{-4}$ M metal nitrate in 1 M nitric acid and $10^{-3}$ M ligand in dichloromethane

The extraction efficiency was studied in terms of the effect of the substituents on the chelating arms with ligands 1-6-4 and 1-6-5 (Figure 2-4). Replacing the ethyl group (1-6-4) with the isopropyl group (1-6-5) did not demonstrate appreciable effect on the extraction performance, in fact, both tripodal chelates showed essentially the same
Figure 2-4. Metal extraction percentages ($%E$) for ligands 1-6-4 and 1-6-5 using $10^{-4}$ M metal nitrate in 1 M nitric acid and $10^{-3}$ M ligand in dichloromethane.

$%E$. Furthermore, both chelates followed the same trend in their affinity along the lanthanide series. Apparently, since the structural modification occurs only at one nitrogen atom, leaving the rest of the chelating group unchanged, the difference in steric and electronic effects is insignificant. The extraction efficiency of the lower side preorganized ligands 1-6-4 and 1-6-5 was slightly higher than the extraction efficiency of 2-2-4 and 3-2-4, although considering experimental error, the difference is negligible.

The effect of the substituents on the triphenoxy methane platform was demonstrated by the results of extraction experiments with 0-6-4 and 1-6-4 (Figure 2-5). The anticipated increase in the extraction ability for the methyl-derivative of the ligand compared to the non-methyl one was not observed, suggesting that the methyl group does not provide enough adjustments in the solubility of the ligand in the organic phase, and it is not bulky enough to restrict flexibility of the binding arm. The slight increase in extraction percentages for several metals in case of 1-6-4 can be neglected when considering the experimental error of approximately 1% for 1-6-4 and 2% for 0-6-4.
Figure 2-5. Metal extraction percentages ($%E$) for ligands 0-6-4 and 1-6-4 using $10^{-4}$ M metal nitrate in 1 M nitric acid and $10^{-3}$ M ligand in dichloromethane.

Extraction investigations have been performed with structurally similar chelates which were not preorganized on a platform. The results show that these ligands are less efficient by several orders of magnitude compared to our ligands. For example, Shimada et al. performed Ln(III) extractions with $N,N'$-dimethyl-$N,N'$-diphenylpyridine-2,6-dicarboxamide (DMDPhPDA) (Figure 2-1), in 1 M HNO$_3$. With 50,000:1 ligand to metal ratio, the distribution values ($D$), on average, were less than $3\times10^{-4}$. In comparison, ligands 0-6-4 and 1-6-4 give average $D$ values of 0.1314 in 1 M HNO$_3$ at 10:1 ligand to metal ratio. Ligands 0-6-4 and 1-6-4 are three orders of magnitude more efficient even when their concentration in the organic phase is 5,000 times smaller. The $D$ values of ligands 0-6-4 and 1-6-4 are shown in Table 2-1.

A considerable increase in extraction efficiency when going from simple pyridine-2,6-dicarboxamides to tris-DPA, is attributed to the fact that $C_3$-symmetric ligands with three arms arranged on a platform, provide a much better coordination environment for the metal compared to the unpreorganized ligand. A total of nine binding sites are
offered by the three tridentate DPA moieties for the Ln(III) binding, affording the preferred TTP geometry. Preorganization has a huge impact on the efficiency of the ligand. The ability to increase the effectiveness of the ligand by a simple modification like this is very important for industrial applications. It enables for a significant reduction in the amount of the material needed, and consequently in decrease of the amount of secondary waste generation which results in the overall decrease in the cost of extraction process.

Another study with an unpreorganized DPA-related ligand $N,N'$-diethyl-$N,N'$-di(p-tolyl)pyridine-2,6-dicarboxamide (EtTPDA) (Figure 2-1) showed that in 3 M HNO$_3$ and with 10,000:1 ligand to metal ratio it extracts Am(III) six times better than Eu(III). Thus, it can be postulated that ligands 0-6-4 and 1-6-4 can considerably increase the An/Ln separation factor. Further investigations with radioactive isotopes $^{241}$Am and $^{152}$Eu are needed.

In order to reduce the impact on the environment, the liquid-liquid extractions should be performed in an environmentally friendly diluent which contains only C, H, O and N atoms. The extraction strength of 1-6-4 was studied in 1-octanol. The experiment was performed under the same conditions as before with 10:1 ligand to metal ratio. The results showed no extraction in this solvent, only Ce(III) and Yb(III) were extracted in 0.7% and 2.0%, respectively. The inability of 1-6-4 to bind lanthanides can be explained in terms of very low solubility of the ligand in this organic diluent.

**Evaluation of Extraction Performance in the Presence of COSAN**

DPAs also demonstrate appreciable synergistic effect, so extractions with ligands 0-6-4 and 1-6-4 were conducted with chlorinated cobalt dicarbollide (COSAN). The extraction experiments in the presence of COSAN followed the same procedure
with slight modifications. Extractions with 0-6-4 and COSAN counterion were performed by Ozge Ozbek.\textsuperscript{37}

Figure 2-6. Metal extraction percentages ($\%E$) for ligands 0-6-4 and 1-6-4 using $10^{-4}$ M metal nitrate in 1 M nitric acid, $10^{-4}$ M ligand and $10^{-3}$ M COSAN in dichloroethane.

Table 2-1. Distribution ratios for extraction experiments with ligands 0-6-4, 1-6-4, 1-6-5, 2-2-4 and 3-2-4.

<table>
<thead>
<tr>
<th></th>
<th>0-6-4 COSAN</th>
<th>1-6-4 COSAN</th>
<th>0-6-4</th>
<th>1-6-4</th>
<th>1-6-5</th>
<th>2-2-4</th>
<th>3-2-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>7.26</td>
<td>17.26</td>
<td>0.18</td>
<td>0.13</td>
<td>0.14</td>
<td>0.11</td>
<td>0.12</td>
</tr>
<tr>
<td>Ce</td>
<td>6.90</td>
<td>24.28</td>
<td>0.14</td>
<td>0.12</td>
<td>0.12</td>
<td>0.11</td>
<td>0.12</td>
</tr>
<tr>
<td>Pr</td>
<td>7.35</td>
<td>17.83</td>
<td>0.13</td>
<td>0.09</td>
<td>0.13</td>
<td>0.08</td>
<td>0.11</td>
</tr>
<tr>
<td>Nd</td>
<td>6.65</td>
<td>26.10</td>
<td>0.13</td>
<td>0.12</td>
<td>0.12</td>
<td>0.05</td>
<td>0.12</td>
</tr>
<tr>
<td>Eu</td>
<td>3.82</td>
<td>21.17</td>
<td>0.14</td>
<td>0.12</td>
<td>0.10</td>
<td>0.09</td>
<td>0.10</td>
</tr>
<tr>
<td>Gd</td>
<td>4.42</td>
<td>19.04</td>
<td>0.12</td>
<td>0.13</td>
<td>0.14</td>
<td>0.11</td>
<td>0.09</td>
</tr>
<tr>
<td>Tb</td>
<td>4.24</td>
<td>22.58</td>
<td>0.14</td>
<td>0.14</td>
<td>0.13</td>
<td>0.09</td>
<td>0.12</td>
</tr>
<tr>
<td>Dy</td>
<td>3.23</td>
<td>46.42</td>
<td>0.14</td>
<td>0.11</td>
<td>0.15</td>
<td>0.09</td>
<td>0.12</td>
</tr>
<tr>
<td>Er</td>
<td>2.17</td>
<td>10.82</td>
<td>0.12</td>
<td>0.16</td>
<td>0.13</td>
<td>0.12</td>
<td>0.09</td>
</tr>
<tr>
<td>Tm</td>
<td>4.03</td>
<td>10.68</td>
<td>0.15</td>
<td>0.11</td>
<td>0.16</td>
<td>0.12</td>
<td>0.13</td>
</tr>
<tr>
<td>Yb</td>
<td>3.64</td>
<td>16.04</td>
<td>0.16</td>
<td>0.13</td>
<td>0.18</td>
<td>0.15</td>
<td>0.08</td>
</tr>
</tbody>
</table>

The extractions were performed in 10:1 ligand to metal ratio using $10^{-4}$ M metal nitrate in 1 M nitric acid and $10^{-3}$ M ligand in dichloromethane. The extraction involving COSAN were performed in 10:1:1 COSAN to ligand to metal ratio using $10^{-4}$ M metal nitrate in 1 M nitric acid, $10^{-4}$ M ligand and $10^{-3}$ M COSAN in dichloroethane.
The presence of this highly hydrophobic counterion has significantly improved the extractions of both ligands. Even at reduced concentration in the organic phase (1×10⁻⁴ M instead of 1×10⁻³ M), both 0-6-4 and 1-6-4 show high extraction power towards lanthanides (Figure 2-6). COSAN acts as a counterion in the lanthanide extractions, helping to solubilize the extracted complex, thus increasing the percent extraction.

Although under the same conditions ligand 1-6-4 shows higher distribution ratios and extraction percentages compared to 0-6-4, the conclusions of the extraction behavior of these ligands cannot be made because extractions in the presence of COSAN were performed by the former member of the group. The possibility of the discrepancy in the extraction results should be taken into account.

Conclusions

The extraction experiments were performed with DPA groups preorganized on the upper and on the lower side of the triphenoxymethane platform. The results demonstrated that substituents on the DPA group and on the tripodal scaffold have no appreciable effect on the ligand performance. The slight difference in the extraction percentages can be attributed to the experimental error. The solubility of the ligand in the organic phase is a determining factor of its efficiency. When COSAN counterion was introduced into the system, the extraction of the metals was increased up to 90%. When 1-octanol was used instead of dichloromethane, the solubility of the ligand was considerably decreased, resulting in very low %E.

The ligands demonstrated slight dependence on the flexibility of the preorganized chelate. A more rigid lower side derivative showed slightly stronger extraction ability compared to the upper side derivative. Nevertheless, taking into account the experimental error, the difference is negligible.
Experimental Section

General Considerations

All reagents were used as received unless otherwise mentioned. Lanthanide salts La(NO$_3$)$_3$·6H$_2$O, Ce(NO$_3$)$_3$·6H$_2$O, Pr(NO$_3$)$_3$·6H$_2$O, Nd(NO$_3$)$_3$·6H$_2$O, Eu(NO$_3$)$_3$·5H$_2$O, Gd(NO$_3$)$_3$·6H$_2$O, Tb(NO$_3$)$_3$·6H$_2$O, Dy(NO$_3$)$_3$·5H$_2$O, Er(NO$_3$)$_3$·5H$_2$O, Tm(NO$_3$)$_3$·5H$_2$O, Yt(NO$_3$)$_3$·5H$_2$O were purchased from Aldrich. Metal solutions in 1M HNO$_3$ were prepared from 18 MΩ Millipore deionized water, TraceMetal-grade HNO$_3$ (Fisher Scientific), and HPLC-grade organic solvents. COSAN was purchased from Katchem spol. s r.o. and used as received. Absorbance of the extracted phase was measured on a Varian Cary 50 UV-vis spectrophotometer. All of the $^1$H and $^{13}$C NMR spectra were recorded on a Varian Gemini-300 spectrometer at 299.95 MHz.

Metal Ion Extractions

The extraction of lanthanides, following a previously reported procedure, was performed using dichloromethane as a solvent for the organic phase.$^{9,24,40}$ The extractability of each cation was calculated as $%E = 100/(A_1 - A)/A_1$), where $A$ is the absorbance of the extracted aqueous phase with the Arsenazo(III) indicator, $A_1$ is the absorbance of the aqueous phase before extraction with the indicator, and $A_0$ is the absorbance of metal-free 1 M nitric acid and the indicator ($\lambda_{Ln(III)} = 665$ nm). The distribution value was determined as $D = [M_{org}]/[M_{aq}]$, where $[M_{org}]$ is the total metal ion concentration in the organic phase and $[M_{aq}]$ is the total metal ion concentration in the aqueous phase. For extraction experiments, 1 M nitric acid was used as an aqueous phase and dichloromethane as an organic phase. Equal amounts of both phases were equilibrated and contacted over the period of approximately 16 hours. Scintillation vials containing 4 ml of $10^{-4}$ M Ln(III) in 1M HNO$_3$, and an equal volume of $1\times10^{-3}$ M ligand in
dichloromethane were placed on an orbital shaker at ambient temperature. Extractions were performed in triplicates on a series of eleven lanthanides with 10:1 ligand to metal ratio. No significant HNO$_3$ coextraction should occur with dichloromethane.$^{29}$ After the vials were removed from the rotator the layers were allowed to separate during one hour period. For the Arsenazo (III) assay, a 6.4×$10^{-4}$ M solution of Arsenazo dye was prepared in pH=2.8 formate buffer. For the extractability determination 2.5 ml of this solution and 1 ml of the aqueous phase after extraction was diluted with pH=2.8 formate buffer in 25 ml volumetric flask. Extractions involving COSAN followed the same procedure except dichloroethane was used instead of dichloromethane as a solvent for the organic phase. Preceding extraction experiment COSAN converted to HCOSAN by preparing 1×$10^{-3}$ M solution in DCE and contacting it with 3 M H$_2$SO$_4$ five times, followed by dissolving 1×$10^{-4}$ M ligand in HCOSAN-dichloroethane solution and equilibrating it with $10^{-4}$ M Ln(III) in 1M HNO$_3$. The tests were performed with 10:1:1 COSAN to ligand to metal ratio.

**Ligand Synthesis**

The preparation of ligands 1-6-4, 1-6-5, 2-2-4 and 3-2-4 was based on the analogous procedure for the preparation of tris-diglycolamides.$^8$ Synthesis of 6-(N,N-diethylcarbamoyl)pyridine-2-carboxylic acid 4 from pyridine-2,6-dicarboxylic acid was previously reported.$^{38,39}$ Compounds 0-6 and 0-6-4 have been prepared by Ozge Ozbek.$^{37}$

Preparation of 6,6',6"-methanetriyltris(4-tert-butyl-2-methylphenol) 1-3.

To a 10 g (60.88 mmol) portion of 4-tert-butyl-2-methylphenol 1-1 in acetonitrile (140 ml), 32 ml (228.31 mmol) of triethylamine was added followed by 8.7 g (91.32 mmol) of magnesium chloride. The solution was stirred under nitrogen for 30 min. Then
12.3 g (410.94 mmol) of paraformaldehyde was added and the reaction mixture was heated to reflux for four hours. The resulting bright yellow material was acidified with 175 ml of 10% HCl and stirred for 45 min. The product was extracted with diethyl ether, washed with brine, dried with magnesium sulfate and concentrated to yellow oil in vacuo to give 1-2. A mixture of 10 g (52.01 mmol) of 5-tert-butyl-2-hydroxy-3-methylbenzaldehyde 1-2 and 17 g (103.5 mmol) of 4-tert-butyl-2-methylphenol 1-1 in 21 ml of methanol was cooled in ice bath. Thionyl chloride (7ml, 96.4 mmol) was added dropwise and the solution was stirred overnight under nitrogen resulting in the formation of 17.87 g (68%) of white product, which was filtered and washed with methanol. $^1$H NMR \((\text{CD}_3)_2\text{SO}\): $\delta$ ppm 1.05 (s, 27 H, Ar-C(CH$_3$)$_3$), 2.08 (s, 9 H, Ar-CH$_3$), 6.58 (s, 1 H, CH), 6.68 (d, $^4$J=2.48 Hz, 3 H, Ar-H), 6.83 (d, $^4$J=2.34 Hz, 3 H, Ar-H). $^{13}$C NMR \((\text{CD}_3)_2\text{SO}\): $\delta$ ppm 17.14 (Ar-C(CH$_3$)$_3$), 31.32 (Ar-C(CH$_3$)$_3$), 33.48 (Ar-CH$_3$), 36.03 (CH), 123.10, 124.40, 124.57, 130.57, 139.96, 149.97 (aromatic).

Preparation of tris(5-tert-butyl-2-methoxy-3-methylphenyl)methane 1-4.

A solution of 5 g (9.94 mmol) of 6,6',6''-methanetriyltris(4-tert-butyl-2-methylphenol) 1-3 and 5 g (15.34 mmol) of cesium carbonate in 50 ml of dimethylformamide was stirred for 30 min followed by the addition of 5 ml (80.3 mmol) of methyl iodide. The reaction mixture was stirred overnight. Cesium carbonate 5 g (15.34 mmol) and methyl iodide 5 ml (80.3 mmol) were added to the solution and it was stirred for two more days. Then 5 ml (80.3 mmol) of methyl iodide was added again and the solution was stirred overnight under nitrogen. The next day product was precipitated with water and recrystallized from DMSO to give 4.78 g (88%) of the material. $^1$H NMR (CDCl$_3$): $\delta$ ppm 1.17 (s, 27 H, Ar-(CH$_3$)$_3$), 2.29 (s, 9 H, Ar-CH$_3$), 3.65 (s, 9 H, O-CH$_3$), 6.56 (s, 1 H, CH),
6.76 (d, $^4J=2.04$ Hz, 3 H, Ar-H), 7.01 (d, $^4J=2.19$ Hz, 3 H, Ar-H). $^{13}$C NMR (CDCl$_3$): $\delta$ ppm 16.58 (Ar-CH$_3$)$_3$, 31.38 (Ar-C(CH$_3$)$_3$), 34.12 (Ar-CH$_3$), 37.69 (CH), 59.92 (O-CH$_3$), 125.56, 125.88, 129.67, 136.11, 145.35, 153.91 (aromatic). Calc. for C$_{37}$H$_{52}$O$_3$: C, 81.57; H, 9.62 %. Found: C, 81.70; H, 10.01 %.

Preparation of tris(2-methoxy-3-methyl-5-nitrophenyl)methane 1-5.

Tris(5-tert-butyl-2-methoxy-3-methylphenyl)methane 1-4, 4.77 g (8.75 mmol) was dissolved in 50 ml of dichloromethane followed by the addition of 4.88 ml (65.66 mmol) of trifluoroacetic acid. Nitric acid, 2.9 ml (65.66 mmol), was charged into addition funnel and added dropwise. After the solution was stirred overnight under nitrogen, the solvent was removed in vacuo to obtain slurry. Methanol was then added and slurry was chilled in a freezer for a few hours. The precipitate was collected by filtration and washed with methanol to yield 1.5 g (34%) of the product. $^1$H NMR (CDCl$_3$): $\delta$ ppm: 2.42 (s, 9 H, Ar-CH$_3$), 3.66 (s, 9 H, O-CH$_3$), 6.54 (s, 1 H, CH), 7.53 (d, $^4J=2.78$ Hz, 3 H, Ar-H), 8.10 (d, $^4J=2.78$ Hz, 3 H, Ar-H). $^{13}$C NMR: $\delta$ ppm: 16.92 (Ar-CH$_3$), 38.71 (CH), 60.42 (O-CH$_3$), 122.52, 126.57, 133.09, 136.33, 143.67, 161.50 (aromatic). Calc. for C$_{25}$H$_{25}$N$_3$O$_9$: C, 58.71; H, 4.93; N, 8.22 %. Found: C, 58.48; H, 4.79; N, 7.98 %.

Preparation of 5,5',5"-methanetriyltris(4-methoxy-3-methylaniline) 1-6.

To a suspension of 8.95 g (17.40 mmol) tris(2-methoxy-3-methyl-5-nitrophenyl)methane 1-5 in absolute ethanol (300 ml), a 34.32 g (524.9 mmol) portion of zinc dust was added. Calcium chloride dihydrate 10.28 g (69.96 mmol) was dissolved in 2 ml of water and added. The mixture was refluxed overnight open to air. When the reflux was complete, conc. NaHCO$_3$ was added to the reaction and the mixture was stirred for 30 min. Zinc was collected by filtration and washed with ethanol. The filtrate was
concentrated in vacuo and the product was extracted with DCM. Organic phase was
dried with MgSO$_4$ and the solvent was removed in vacuo to give 7.0 g of the product
(95%). $^1$H NMR (DMSO-d$_6$): $\delta$ ppm 2.08 (s, 9 H, Ar-CH$_3$), 3.44 (s, 9 H, O-CH$_3$), 4.59 (s,
6 H, Ar-NH$_2$), 5.93 (d, $J$=2.63 Hz, 3 H, Ar-H), 6.06 (s, 1 H, CH), 6.21 (d, $J$=2.63 Hz, 3 H,
Ar-H). $^{13}$C NMR (DMSO-d$_6$): $\delta$ ppm 16.09 (Ar-CH$_3$), 37.10 (CH), 59.32 (O-CH$_3$), 113.67,
114.32, 129.78, 137.38, 143.54, 146.75 (aromatic). HR DIP-Cl MS m/z [M+H]$^+$ =
421.2369. Theoretical m/z [M+H]$^+$ = 421.2400.

Preparation of $N^2,N^2,N^2'-(5,5',5''$-methanetriyltris(4-methoxy-3-methylbenzene-
5,1-diyl))tris-($N^6,N^6$-diethylpyridine-2,6-dicarboxamide) 1-6-4.

The procedure for the preparation of 1-6-4 was adopted from the synthesis of tris-
diglycolamides$^{8,41}$ and tris-DPAs$^{37}$ according to the reported procedure. To a solution of
0.5 g (1.18 mmol) 5,5',5'"-methanetriyltris(4-methoxy-3-methylaniline) 1-6 in 12.5 ml of
DMF, 1.25 ml (7.18 mmol) of N,N-diisopropylethylamine, 2.2 g of PyBOP (4.22 mmol)
and 0.8 g of 6-(diethylcarbamoyl)picolinic acid 4 (3.6 mmol) were added. The mixture
was stirred overnight under nitrogen followed by addition of 50 ml of 10% HCl solution.
The precipitate that formed after stirring for one hour was extracted with ethyl acetate,
washed with 1M NaOH and brine and then dried with MgSO$_4$. After the solvent was
removed in vacuo, the product was obtained in 71% yield (0.86 g). $^1$H NMR (CDCl$_3$): $\delta$
ppm: 1.03 - 1.16 (m, 18 H, overlapping signals NCH$_2$CH$_3$, NCH$_2$CH$_3$) 2.37 (s, 9 H, Ar-
CH$_3$) 3.22 (q, $J$=6.91 Hz, 6 H, NCH$_2$CH$_3$) 3.39 (q, $J$=6.91 Hz, 6 H, NCH$_2$CH$_3$) 3.68 (s, 9
H, Ar-OCH$_3$) 6.52 (s, 1 H, C-H) 6.57 (d, $J$=2.63 Hz, 3 H, Ar-H) 7.75 (dd, $^3J$=7.74,
$^4J$=1.17 Hz, 3 H, Py-H) 7.98 (t, $J$=7.81 Hz, 3 H, Py-H) 8.07 (d, $J$=2.48 Hz, 3 H, Ar-H)
8.28 (dd, $^3J$=7.74, $^4J$=1.02 Hz, 3 H, Py-H). $^{13}$C NMR (CDCl$_3$): $\delta$ ppm 12.59, 14.39,
Preparation of \( N^2,N^2,N^2''-(5,5',5''\text{-methanetriyltris(4-methoxy-3-methylbenzene-5,1-diyl)}\text{tris-(N}^6,N^6\text{-diisopropylpyridine-2,6-dicarboxamide)} \) \( 1-6-5 \)

The procedure for the preparation of \( 1-6-5 \) followed the same synthetic route as in case of \( 1-6-4 \). A weighted amount of \( 5,5',5''\text{-methanetriyltris(4-methoxy-3-methylaniline)} \) \( 1-6 \) (0.43 g, 1.18 mmol) was dissolved in 30 ml of DMF; 1.4 ml (7.86 mmol) of N,N-diisopropylethylamine, 2.2 g of PyBOP (4.33 mmol) and 0.98 g of 6-(diethylcarbamoyl)picolinic acid 5 (3.90 mmol) were added. The mixture was stirred overnight under nitrogen followed by addition of 50 ml of 10% HCl solution. The precipitate that formed after stirring for one hour was extracted with ethyl acetate, washed with 1M NaOH and brine and then dried with MgSO\(_4\). After the solvent was removed in vacuo, the product was obtained in 68% yield (0.89 g). 

\(^1\)H NMR (CDCl\(_3\)): \( \delta \) ppm 1.03 (d, \( J=6.79 \) Hz, 18 H, NCH(CH\(_3\))\(_2\)), 1.34 (d, \( J=6.51 \) Hz, 18 H, NCH(CH\(_3\))\(_2\)), 2.37 (s, 9 H, Ar-CH\(_3\)), 3.32 - 3.43 (m, 3 H, NCH(CH\(_3\))\(_2\)), 3.69 (s, 9 H, Ar-OCH\(_3\)), 3.84 - 3.95 (m, 3H, NCH(CH\(_3\))\(_2\)), 6.43 (d, \( J=2.5 \) Hz, 3 H), 6.45 (s, 1 H, CH), 7.69 (dd, \( ^3J=7.79 \), \( ^4J=0.99 \) Hz, 3 H, Py-H), 7.97 (t, \( J=7.79 \) Hz, 3 H, Py-H), 8.15 (d, \( J=2.5 \), 3 H, Ar-H), 8.25 (dd, \( ^3J=7.79 \) Hz, \( ^4J=70.99 \), Hz 3 H, Py-H), 9.66 (s, 3 H, Ar-NH). 

\(^{13}\)C NMR (CDCl\(_3\)): \( \delta \) ppm 16.65, 20.23, 20.66, 46.32, 50.54 (aliphatic); 60.19 (O-CH\(_3\)); 118.44, 120.96, 122.24, 125.88, 132.20, 133.18, 137.13, 138.88, 147.95, 152.88, 154.41 (aromatic); 160.69,

Synthesis of 2,2',2"-(6,6',6"-methanetriyltris(4-tert-butyl-2-methylbenzene-6,1-diyl)tris(oxy)) triacetonitrile 2-1

The 2-1 has been prepared according to the previously reported procedure with slight modifications. A weighed amount of 1-6 (5.0 g, 9.94 mmol) was dissolved in 130 ml of acetone. Then 13.82 g of K$_2$CO$_3$ (100 mmol) and 15.0 g of NaI (100 mmol), were added to the reaction mixture along with 7 ml (110 mmol) of chloroacetonitrile. The reaction was allowed to reflux under nitrogen overnight. Yield 30% 1.73 g. $^1$H NMR (CDCl$_3$): δ ppm 1.19 (s, 27 H, Ar-C(CH$_3$)$_3$), 2.37 (s, 9 H, Ar-CH$_3$), 4.15 (s, 6 H, Ar-O-CH$_2$-CN), 6.40 (s, 1 H, C-H), 6.86 (d, $J$=2.48 Hz, 3 H, Ar-H), 7.12 (d, $J$=2.34 Hz, 3 H, Ar-H). $^{13}$C NMR (CDCl$_3$): δ = 17.10, 31.28, 34.34, 37.72, 57.28 (aliphatic); 115.54 (CN); 125.57, 127.42, 130.94, 135.05, 147.91, 151.47 (aromatic).

Synthesis of 2,2',2"-(6,6',6"-methanetriyltris(4-tert-butyl-2-methylbenzene-6,1-diyl)tris(oxy)) triethan amine 2-2

The preparation of 2-2 followed previously reported procedure for the preparation of the tripodal platform with two carbon linker. After measuring exactly 3.03 g (5.24 mmol) of 2-1, it was dissolved in 20 ml of DCM and added dropwise to the 2.6 g (67.5 mmol) of LAH (LiAlH$_4$) in 30 ml of DCM. After stirring the reaction overnight, 4.5 ml of 5% NaOH was added and stirred for 30 min. affording 2.52 g of product in 76% yield. $^1$H NMR (CDCl$_3$): δ ppm 1.17 (s, 27 H, Ar-C(CH$_3$)$_3$), 2.25 (s, 9 H, Ar-CH$_3$), 2.86 (t, $J$=5.11 Hz, 6 H, Ar-O-CH$_2$-CH$_2$), 3.31 (t, $J$=5.11 Hz, 6 H, Ar-O-CH$_2$-CH$_2$), 6.76 (s, 1 H, C-H), 6.92 (d, $J$=2.48 Hz, 3 H, Ar-H), 6.99 (d, $J$=2.48 Hz, 3 H, Ar-H). $^{13}$C NMR (CDCl$_3$): δ =
Preparation of $N^2,N^2,N^2''-(2,2',2''-(6,6',6''-\text{methanetriyl})tris(4\text{-tert-butyl}-2-
\text{methylbenzene-6,1-diyl})\text{tris(oxy)})\text{tris(ethane-2,1-diyl})\text{tris}(N^6,N^6\text{-diethylpyridine-2,6-
dicarboxamide})$ 2-2-4

The preparation of upper side functionalized 2-2-4 was performed similar to 1-6-4 and 1-6-5. $^{7,37,42}$ 0.5 g of 6-(diethylcarbamoyl)picolinic acid 4 (2.25 mmol), 1.3 g (2.5 mmol) of Pybop and 0.8 ml (4.5 mmol) of amine to 25 ml of anhydrous DMF was stirred for 30 min. prior to addition of 0.41 g of amine 2-2 (0.65 mmol). The reaction was stirred for 22 hours followed by addition of 100 ml of 10% HCl. After contacting with HCl for 1 hour, the precipitate that formed shortly after the addition of HCl was filtered and dissolved in diethyl ether. The ligand solution in ether was washed with 1 M NaOH and brine. The organic layer was dried with MgSO$_4$, and the solvent was partially removed. Treatment with pentane resulted in the precipitation of the white product in 63 % yield (0.51 g). $^1$H NMR (CDCl$_3$): $\delta$ ppm 1.01 (t, $J=7.01$ Hz, 9 H, NCH$_2$CH$_3$), 1.08 (s, 27 H, Ar-C(CH$_3$)$_3$), 1.12 (t, $J=7.01$ Hz, 9 H, NCH$_2$CH$_3$), 2.07 (s, 9 H, Ar-CH$_3$), 3.20 (q, $J=7.01$ Hz, 6 H, NCH$_2$CH$_3$), 3.36 - 3.51 (m, 12 H, O-CH$_2$CH$_2$-N), 3.66 (q, $J=5.06$ Hz, 6 H, NCH$_2$CH$_3$), 6.46 (s, 1 H, CH), 6.82 (d, $J=2.19$ Hz, 3 H, Ar-CH$_3$), 6.89 (d, $J=2.19$ Hz, 3 H, Ar-CH$_3$), 7.60 (d, $J=7.74$ Hz, 3 H, Py-H), 7.85 (t, $J=7.81$ Hz, 3 H, Py-H), 8.16 (d, $J=7.74$ Hz, 3 H, Py-H). $^{13}$C NMR (CDCl$_3$): $\delta$ ppm: 12.65, 14.24, 16.50, 31.19, 33.99, 40.04, 43.00, 70.64 (aliphatic); 122.61, 125.28, 125.61, 125.89, 129.65, 136.00, 138.29, 145.63, 148.42, 152.22, 153.52 (aromatic); 163.67, 167.41 (C=O). HR ESI MS [M+H]$^+$ =
Preparation of 2,2',2''-(3,3',3''-(6,6',6''-methanetriyltris(4-tert-butyl-2-methylbenzene-6,1-diyl)tris-(oxy))tris(propane-3,1-diyl)trisioindoline-1,3-dione 3-1

Preparation of 3-1 was slight modified from the previously reported procedure for the preparation of similar compounds with different substituents.\(^7,8,37\) Suspension of 5 g (9.94 mmol) of 1-6 in 100 ml of DMF was stirred under nitrogen for 30 min. followed by addition of 27.54 g (84.54 mmol) of Cs\(_2\)CO\(_3\). After stirring the mixture for 1 hour, 22.65 g (84.54 mmol) of phthalimide was added and the mixture was refluxed for 6 days at 80-85 °C. Upon the completion of the reaction, the mixture was cooled to room temperature and poured into chilled H\(_2\)O which resulted in the formation of the white precipitate. The solvent was then partially removed and the precipitate was extracted with Et\(_2\)O. The organic layer was washed with 15% HCl, dried with MgSO\(_4\) and removed under vacuum giving 7.19 g of product (68% yield). \(^1\)H NMR (CDCl\(_3\)) δ ppm: 1.18 (s, 27 H, Ar-C(CH\(_3\)\(_3\))), 2.07 (m, 6 H, O-CH\(_2\)CH\(_2\)CH\(_2\)), 2.24 (s, 9 H, Ar-CH\(_3\)), 3.35 (t, \(J=6.06\) Hz, 6 H, CH\(_2\)CH\(_2\)CH\(_2\)N), 3.88 (t, 6 H, O-CH\(_2\)CH\(_2\)CH\(_2\)), 6.85 (s, 1 H, C-H), 6.93 (d, \(J=2.34\) Hz, 3 H, Ar-H), 6.99 (d, \(J=2.48\) Hz, 3 H, Ar-H), 7.70 - 7.77 (m, 6 H, Ar-H), 7.84 - 7.89 (m, 6 H, Ar-H).

Preparation of 3,3',3''-(6,6',6''-methanetriyltris(4-tert-butyl-2-methylbenzene-6,1-diyl)tris-(oxy))tripropan-1-amine 3-2

The procedure for the preparation of the amine with three carbon linker 3-2 was slightly modified from the previously reported route.\(^8,29,37\) After dissolving 2 g of 3-1 (1.88 mmol) in 60 ml of ethanol, 0.4 ml of hydrazine (7.51 mmol) was added to the
same reaction vessel. The mixture was heated to reflux for 24 hrs and was poured into chilled H$_2$O, resulting in the formation of the white precipitate. The precipitate was filtered and recrystallized from acetonitrile giving 1.09 g of solid material in 86% yield.

$^1$H NMR (CDCl$_3$) δ ppm: 1.10 (s, 27 H, Ar-C(CH$_3$)$_3$), 1.91 - 2.03 (m, 6 H, O-CH$_2$CH$_2$CH$_2$), 2.18 (s, 9 H, Ar-CH$_3$), 3.06 - 3.24 (overlapping signals, 12 H, CH$_2$CH$_2$CH$_2$N and O-CH$_2$CH$_2$CH$_2$), 5.35 (s, 6 H, N-H), 6.60 (s, 1 H, C-H), 6.87 (d, J=1.90 Hz, 3 H, Ar-H), 6.92 (d, J=1.75 Hz, 3 H, Ar-H). $^{13}$C NMR (CDCl$_3$) δ ppm: 16.84, 29.31, 31.34, 34.17, 38.39, 52.78, 75.98 (aliphatic); 128.96, 129.98, 132.27, 136.21, 145.98, 151.94 (aromatic).

Preparation of $N^2,N^2,N^2''-(3,3',3''-(6,6',6''-methanetriyltris(4-tert-butyl-2-methylbenzene-6,1-diyl)-tris(oxy))tris(propane-3,1-diyl))tris(N$_6$N$_6$-diethylpyridine-2,6-dicarboxamide) 3-2-4

1.2 g (4.93 mmol) of 6-(diethylcarbamoyl)picolinic acid 4, 1.8 ml (10.64 mmol) of diethyiisopropyl amine and 3 g (5.85 mmol) of Pybop were dissolved in 25 ml of anhydrous DMF and stirred for 30 min., then 1 g (1.48 mmol) of 3-2 amine was added and the reaction was stirred overnight. Then 100 ml of 10% HCl was added to the mixture and stirred for 1 hour, the precipitate was filtered, dissolve in ether, wash with 1 M NaOH and brine. The organic layer was dried with MgSO$_4$ and partially evaporated. Then it was treated with pentane, which produced a white precipitate in 25 % yield (0.48 g). $^1$H NMR (CDCl$_3$) δ ppm: 1.12 (t, J=7.23 Hz, 9 H, N-CH$_2$CH$_3$), 1.16 (s, 27 H, Ar-C(CH$_3$)$_3$), 1.21 (t, J=7.30 Hz, 9 H, N-CH$_2$CH$_3$), 1.90 - 2.01 (m, J=6.57 Hz, 6 H, O-CH$_2$CH$_2$CH$_2$), 2.22 (s, 9 H, Ar-CH$_3$), 3.25 (q, J=6.82 Hz, 6 H, N-CH$_2$CH$_3$), 3.39 (t, J=5.92 Hz, 6 H, O-CH$_2$CH$_2$CH$_2$), 3.49 (q, J=7.06 Hz, 6 H, N-CH$_2$CH$_3$), 3.58 - 3.67 (m, 6 H, O-
$\text{CH}_2\text{CH}_2\text{CH}_2$, 6.75 (s, 1 H, C-H), 6.91 (d, $J$=2.34 Hz, 3 H, Ar-H), 6.96 (d, $J$=2.34 Hz, 3 H, Ar-H), 7.62 (d, $J$=7.74 Hz, 3 H, Ar-H), 7.90 (t, $J$=7.38 Hz, 3 H, Py-H), 8.17 (d, $J$=8.03 Hz, 3 H, Py-H). $^{13}$C NMR (CDCl$_3$) δ ppm: 12.76, 14.02, 14.35, 16.80, 30.15, 31.34, 34.10, 37.20, 40.03, 43.09, 52.75, 69.62 (aliphatic); 122.68, 125.07, 125.74, 129.76, 136.46, 138.39, 145.36, 148.86, 152.72, 153.49 (aromatic); 163.73, 167.79 (C=O). HR ESI MS [M+H]$^+$ = 1286.7932, [M+Na]$^+$ = 1308.7761. Theoretical m/z [M+H]$^+$ = 1286.7952, [M+Na]$^+$ = 1308.7771
CHAPTER 3
EXTRACTION OF RARE EARTH METALS WITH TRIPODAL THIO-DIPICOLINIC ACID DERIVATIVE

Introduction

In 1954 Diamond et al. reported that actinides have higher affinity for ligands containing soft-donor atoms.\textsuperscript{4} It was postulated that the more extended 5f orbitals of actinides result in a more covalent behavior of these elements. In addition, 6s orbitals of actinides, unlike 4f orbitals of lanthanides, can be involved in bond formation.\textsuperscript{43} Increased covalency is expected to be associated with a more exothermic heat for complexation; however, the analysis of the enthalpies of the complex formation revealed no clear indication of the covalent contribution to the actinide binding.\textsuperscript{3} Nonetheless, the soft-donor hypothesis has been further exploited and applied in the development of various extraction systems containing soft-donor atoms such as nitrogen and sulfur.

Cyanex Extractant

Commercially available extractant Cyanex 301 was originally developed for the selective extraction of Zn(II) at pH ≤ 2 from effluents which also contain Ca(II).\textsuperscript{44} In 1996, Zhu et al. used purified Cyanex 301 for separation of Am(III) and Eu(III) and reported the $SF_{\text{Am/Eu}}$ of 5900. The extraction was performed with the trace amounts of $^{241}$Am(III) and $^{152-154}$Eu(III) with 0.5 M ligand in kerosene. The pH range 2.5-4.5 of the aqueous phase was adjusted with NaOH and HNO\textsubscript{3} at a constant ionic strength of 1 M NaNO\textsubscript{3}.\textsuperscript{45}

Hill et al. (0.5 M purified Cyanex 301 in $n$-dodecane), showed a $SF_{\text{Am/Eu}}$ of ~6000 at pH = 3.4. However, when 0.1 M Eu(NO\textsubscript{3})\textsubscript{3} was added to the extraction mixture at pH = 3.7, the $SF_{\text{Am/Eu}}$ greater than 30,000 was reported.\textsuperscript{45,46} Hill group did not provide the
explanation for the increase in the SF upon the addition of the 0.1 M Eu(NO₃)₃.

Bhattacharyya et al. explained that such an unusually high separation factor in nitrate medium is due to Eu(III) having a higher extraction constant (Kₑₓ) under these conditions. The bond between M(III) and NO₃⁻ ion is stronger in case of Eu(III) compared to Am(III), thus at lower Cyanex concentration (0.1 M) and increased NO₃⁻ concentration, Eu(III) preferentially binds nitrate ions, while softer Am(III) is selectively extracted by purified Cyanex 301.¹⁶

Organophosphorus Cavitands

The 1:3 metal to ligand stoichiometry of Cyanex ligands is very important because it enables the preorganization of the ligand on a platform. As expected, Eu(III) was not extracted with both rigid and flexible cavitand 3-1 and 3-2 (Figure 3-1) since it contains soft donor sulfur. When competition extraction was performed with trace amounts of Am(III) and Eu(III) (< 10⁻⁶ M) under the same conditions, the more rigid cavitand demonstrated surprisingly low distribution ratios for Am(III) and Eu(III) and a very poor SFₐm/Eu of 1.7, while the cavitand 3-2 showed no extraction at all. The authors suggested that the acid function of Cyanex 301 is the reason for the very high Am(III)/Eu(III) separation factor.⁴⁵ Ligands 3-1 and 3-2 associate via ion-dipole
interactions, thus the metal extraction is very poor. Even addition of synergists did not improve the SF, confirming that the acid function is essential for the high extraction performance of the sulfur bearing ligands.\(^47\)

Compound 3-3 preferentially extracted Eu(III) with the \(SF_{\text{Eu/Am}}\) \(\approx 5\) which is 12 times higher than extractions by Cyanex 272 alone. Observation suggests that the ionic interactions are essential for the application of sulfur-containing extractants and that the preorganization of the Cyanex reagents can significantly increase the SF.\(^47\)

**Stability of Cyanex Ligands**

Despite very high separation factors, the industrial application of Cyanex 301 extractant is limited. Significant degradation and decrease in separation efficiency of the pure Cyanex 301 occurs after the exposure to nitric acid at a concentration greater than 2 M\(^48\) and a dose of \(\gamma\) radiation greater than \(1 \times 10^5\) Gy.\(^49\)

IR spectroscopy showed that the organic phases were unchanged after contact with nitric acid at a concentration up to 2 M.\(^60\) At higher concentrations, the main oxidation products are nitrogen dioxide, elemental sulfur and oxo-analogues of the reagent: \(R_2P(S)OH\) (Cyanex 302) and \(R_2P(O)OH\) (Cyanex 272).\(^48\) Oxidation

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**Figure 3-1.** Structures of phosphane sulfide and phosphinic acid cavitands. 3-1: tetrakis-(diphenylmethylphosphane sulfide); 3-2: tetrakis(butoxydiphenyl methylphosphane sulfide); 3-3: tetrakis(phenylmethylphosphinic acid).
complicates the Am(III)/Eu(III) separation because the amount of the starting material decreases, and oxidation products can participate in extraction. After γ-irradiation of 7×10^5 Gy the SF_{Am/Eu} was shown to decrease by two orders of magnitude. However, purified Cyanex 301 was shown to be more resistant to radiation. After a dose of 10^5 Gy the damage percentage in xylene was 54% and 94% for purified and non-purified reagent, respectively.

Results and Discussion

Ligand Preparation

Sulfurization of DPA derivatives yields a ligand that is stable to hydrolysis and has more covalent character, which implies high SF_{Am/Eu}. Compound 1-6-5-S was prepared by thionating previously synthesized ligand 1-6-5 with the Lawesson’s Reagent. Lawesson’s Reagent is widely used as a sulfurization agent along with P_2S_5.

Scheme 3-1. Synthesis of tris-DPAS ligand 1-6-5-S. Reflux with Lawesson’s Reagent in benzene overnight.
Synthesis was carried out in benzene; upon completion of the reaction, solvent was evaporated and the ligand was dissolved in DMF followed by addition of 10% HCl. The solution was stirred for 30 min and the precipitate was collected by filtration and washed with ethanol to remove excess Lawesson’s Reagent. Substitution of oxygen atoms for sulfur was verified by NMR, HR MS and IR spectroscopy. Comparison of $^1$H NMR spectrum of the ligand before and after thionation shows significant chemical shifts for the characteristic signals: central carbon peak shifted from 6.45 ppm to 6.52 ppm; Ar-$H$ peaks are shifted from 6.43 and 8.15 to 6.88 and 8.42; Py-$H$ signals from 7.69, 7.97 and 8.25 to 7.55, 7.84 and 8.66; the N-$H$ peak shifted from 9.66 ppm to 11.55 ppm. IR spectrum shows close match in stretches between 1-6-5-S and free diethylthiopicolinic acid: 418 vs. 414, 508 vs. 501, 558 vs. 557, 690 vs. 685, 723 vs. 724, 776 vs. 770, 818 vs. 816, 990 vs. 980, 1096 vs. 1094, 1145 vs. 1144, 1196 vs. 1196, 1295 vs. 1292, 1440 vs. 1443, 1508 vs. 1506, and 1580 vs. 1580 respectively.

**Evaluation of Extraction Performance**

Extraction experiment was performed in a similar way as described for DPA extractants. It was anticipated that the $%E$ will decrease since ligand contains soft sulfur donor atoms, which prefer binding to An(III) rather than Ln(III). The comparison of extraction performance of 1-6-5 and 1-6-5-S shows a decrease in $%E$ (Figure 3-2) from 12 to 8 % on average not considering the experimental error. Neither ligand has selectivity for any particular metal along the lanthanide series. Results of extraction experiment is shown in Table 3-1.
Figure 3-2. Metal extraction percentages (%E) for ligands 1-6-5 and 1-6-5-S using $10^{-4}$ M metal nitrate in 1 M nitric acid and $10^{-3}$ M ligand in dichloromethane.

Conformation that Ln(III) extract less with soft donor ligands is encouraging because it can be postulated that ligand 1-6-5-S will be efficient in extraction of An(III) and will produce high SF. Moreover, since the %E for Ln(III) did not reduce to zero, the ligand will be capable of extracting both actinides and lanthanides. Additional studies with actinides are required.

Table 3-2. Percent extraction (%E), percent error (% error) and distribution ratios (D) for extraction experiments with ligands 1-6-5-S and 1-6-5

<table>
<thead>
<tr>
<th></th>
<th>1-6-5-S</th>
<th></th>
<th>1-6-5</th>
<th></th>
<th>1-6-5</th>
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<tr>
<td></td>
<td>%E</td>
<td>% error</td>
<td>D</td>
<td>%E</td>
<td>% error</td>
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<tr>
<td>La</td>
<td>7.25</td>
<td>2.0</td>
<td>0.07</td>
<td>12.08</td>
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<tr>
<td>Ce</td>
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<td>0.8</td>
<td>0.08</td>
<td>10.81</td>
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<tr>
<td>Pr</td>
<td>8.94</td>
<td>1.6</td>
<td>0.09</td>
<td>11.63</td>
<td>1.0</td>
</tr>
<tr>
<td>Nd</td>
<td>9.87</td>
<td>0.9</td>
<td>0.10</td>
<td>10.62</td>
<td>1.8</td>
</tr>
<tr>
<td>Eu</td>
<td>9.93</td>
<td>0.7</td>
<td>0.10</td>
<td>9.00</td>
<td>1.1</td>
</tr>
<tr>
<td>Tb</td>
<td>8.30</td>
<td>1.0</td>
<td>0.08</td>
<td>12.47</td>
<td>1.6</td>
</tr>
<tr>
<td>Dy</td>
<td>7.50</td>
<td>0.5</td>
<td>0.09</td>
<td>11.80</td>
<td>1.8</td>
</tr>
<tr>
<td>Gd</td>
<td>7.20</td>
<td>2.0</td>
<td>0.07</td>
<td>13.03</td>
<td>1.6</td>
</tr>
<tr>
<td>Er</td>
<td>7.00</td>
<td>0.6</td>
<td>0.07</td>
<td>11.35</td>
<td>0.7</td>
</tr>
<tr>
<td>Tm</td>
<td>8.54</td>
<td>0.7</td>
<td>0.09</td>
<td>13.99</td>
<td>1.5</td>
</tr>
<tr>
<td>Yb</td>
<td>7.48</td>
<td>2.8</td>
<td>0.08</td>
<td>15.09</td>
<td>2.1</td>
</tr>
</tbody>
</table>

The extractions were performed in 10:1 ligand to metal ratio using $10^{-4}$ M metal nitrate in 1 M nitric acid and $10^{-3}$ M ligand in dichloromethane.
Solid state studies with ligands containing similar metal binding site formed a
dimer with NiCl$_2$. The bond length between Ni$^{2+}$ and nitrogen on the pyridine was
2.043(6) Å and C=S bond was 1.656(8) Å. In a analogous complex containing oxygen
donor atoms instead of sulfur, the bond lengths were 2.023(3) Å for Ni-N bond and
1.252(5) Å for C=O bond.$^{56}$ As expected, C=O bond is shorter compared to C=S bond.
A ligand containing thiazolyl units at 2 and 4 positions of the pyridine ring forms a
dinuclear double helicate complex with Cu$^{2+}$. Both Cu ions are coordinated by two
bidentate pyridyl-thiazolyl fragments from each ligand through nitrogen atoms instead of
sulfur. Interestingly, pyridine nitrogen is not involved in coordination to Cu, and Cu
thiazolyl N bond lengths vary from 1.956(5) Å to 1.983(5) Å.$^{57}$

Conclusions

Substitution of oxygen atoms of the DPA-based ligand for sulfur provided a ligand
with more covalent character, resulting in lower $\%E_{Ln}$. Since the ligand was still able to
extract lanthanides, it is expected that it will extract actinides as well. It is also expected
that the ligand will be preferentially extracting An(III) over Ln(III). A study with
transuranium elements would be able to answer this question. Also a study with
COSAN would be a benefit: it is expected that COSAN counterion will be able to
considerably improve $\%E$. Ligand 1-6-4 removed over 95% Ln(III) after first extraction,
similar behavior is expected for 1-6-5 since two ligands structurally resemble each
other.

Experimental Section

General Considerations

All reagents were used as received unless otherwise mentioned. Lanthanide salts
were purchased from Aldrich. Metal solutions in 1M HNO$_3$ were prepared form 18 MΩ
Millipore deionized water, TraceMetal-grade HNO₃ (Fisher Scientific), and HPLC-grade organic solvents. Absorbance of the extracted phase was measured on a Varian Cary 50 UV-vis spectrophotometer. All of the ¹H and ¹³C NMR spectra were recorded on a Varian Gemini-300 and Mercury-300 spectrometer at 299.95 MHz.

**Metal Ion Extractions**

The extraction of lanthanides, following a previously reported procedure, was performed using dichloromethane as a solvent for the organic phase. The extractability of each cation was calculated as 

\[ \%E = \frac{100}{(A_1 - A) / (A_1 - A_0)} \]

\[ \lambda_{\text{Ln(III)}} = 665 \text{ nm} \]

Distribution values were determined as 

\[ D = \frac{[M_{\text{org}}]}{[M_{\text{aq}}]} \]

Extraction procedure was the same as in case of DPA derivatives. Phases were contacted over 16 hours, extractions were performed in triplicates on a series of eleven lanthanides with 10:1 ligand to metal ratio. After the vials were removed from the rotator the layers were allowed to separate during one hour.

**Ligand Synthesis**

Preparation of \( N^2,N^2',N^2''-(5,5',5''-\text{methanetriyl})tris(4-\text{methoxy}-3-\text{methylbenzene}-5,1-diyl})tris(N^6,N^6'-\text{diisopropylpyridine}-2,6-bis(carbothioamide)) \). **1-6-5-S**

Previously prepared ligand **1-6-5** 0.25g (0.22 mmol) was dissolved in 8.2 ml of benzene and 1.08 g (2.68 mmol) of Lawesson’s Reagent has been added. The reaction was heated to reflux overnight. After solvent was removed, the ligand was dissolved in 10 ml of DMF followed by the addition of 100 ml of 10% HCl solution. The reaction mixture was stirred for 30 min, resulting in the formation of the precipitate, which was collected by filtration and washed with ethanol to remove excess Lawesson’s Reagent to give 0.14 g (52%) of yellow material. ¹H NMR (CDCl₃) δ ppm: 1.06 (d, \( J=6.57 \) Hz, 32 H, NCH(CH₃)₂), 2.38 (s, 9 H, Ar-CH₃), 3.67 (s, 9 H, Ar-OCH₃), 3.77 - 3.92 (m, 6 H, Ar-OCH₃).
NCH(CH$_3$)$_2$, 6.52 (s, 1 H, CH), 6.88 (br. s., 3 H, Ar-H), 7.55 (dd, $J$=7.74, 0.88 Hz, 3 H, Py-H), 7.84 (t, $J$=7.89 Hz, 3 H, Py-H), 8.42 (br. s., 3 H, Ar-H), 8.66 (dd, $J$=7.74, 0.88 Hz, 3 H, Py-H), 11.55 (s, 3 H, Ar-NH). $^{13}$C NMR (CDCl$_3$) $\delta$ ppm: 16.77, 19.00, 22.31, 38.52, 60.19 (aliphatic); 121.75, 123.57, 123.63, 125.05, 131.86, 134.16, 137.21, 138.27, 149.23, 154.51 (aromatic), 157.77 (C=S). HR ESI MS [M+H]$^+$ = 1214.4669, [M+Na]$^+$ = 1236.4495. Theoretical m/z [M+H]$^+$ = 1214.4703, [M+Na]$^+$ = 1236.4522.
CHAPTER 4
C₃-SYMMETRIC TRIPHENOXYMETHANE PLATFORM FUNCTIONALIZED WITH PYRIDINE N-OXIDE

Introduction

Since CMPO ligands have been very successful extractants, it seemed that other bidentate hard donor organic chelates will also have good extraction potential. One of these hard donor ligands are N-oxide derivatives. And although, like CMPO they contain two hard donor atoms, they have not received as much attention as the CMPO chelates.

N-oxide based ligands are considered to have $sp^2$ hybridized oxygen, which is in conjugation with the aromatic pyridine ring. As a result of conjugation and high electronegativity of the oxygen, the basicity of N-oxides is lower compared to their unoxidized analogs. However, recent studies have shown that N-oxides can undergo $sp^2 \rightarrow sp^3$ rehybridization, especially upon coordination to the Lewis and Bronsted-Lowry acids. Low basicity of N-oxides is combined with their high nucleophilic character, which is due to the resonance structures where the double N-O bond character prevails. When electrophilic agent attacks N-oxide, first the $sp^2$ orbital forms the bond O-E⁺, however, due to the polarization and elongation of the N-O bond, oxygen becomes $sp^3$ hybridized. The loss of conjugation can result in the decrease in stability of the ligand-electrophile complex. In case the electrophile is lanthanide or actinide metal ion this can result in the unsuccessful extraction attempt.

N-oxides have found limited application in the sequestration of f-elements. One of the rare examples includes phosphinopyridine N-oxide ligands where the $D$ values have been measured as a function of the nitric acid concentration. The increase in the $D$ ratio was up to 1M HNO₃, which is explained by the increase in competitive extraction of
HNO₃ above 1M. The tridentate derivative of phosphinopyridine N-oxide was also shown to have 10³ higher distribution ratios ($D \approx 11$) compared to the bidentate derivative ($D \approx 0.011$) due to decreased basicity of the P=O group and steric hindrance of the N-O oxygen.⁵⁹

Extraction behavior of unoxidazed derivatives of N-oxide ligands received more attention, they were studied as single molecules and as preorganized chelates.⁶⁰-⁶⁴ For example, N-butylpicolinamide exhibited $D_{Eu}$ and $D_{Am}$ below 0.003 in o-nitrophenyl hexyl ether, but $D_{Eu}$ more than 300 and $D_{Am}$ of 21.4 when 0.02 M of BrCosan was added. The highest $SF_{Am/Eu}$ of 0.9 was achieved at 0.003 M BrCosan. Calixarene-based ligands were superior to the N-butylpicolinamide. The $SF_{Am/Eu}$ greater than 10 have been observed. The trends in the extraction performance were subtle, but the it was noticed that calix[8]arenes were more efficient than calix[6]arenes and calix[4]arenes; the longer spacer increased the $D$ ratio but decreased $SF$. For the upper rim calixarenes shorter spacer group resulted in higher selectivity. The upper rim calix[4]arene gave rise to the highest $SF_{Am/Eu}$ of 13.8 in the presence of 3×10³ M BrCosan. The thio derivative of calixarenes picolinamide was unsuccessful in the separation ($SF_{Am/Eu} = 0.9$, $D_{Eu} = 0.23$ and $D_{Am} = 0.20$).⁶⁵

Despite limited data on extraction behavior, Ln(III)–N-oxide complexes have been studied intensively. N-oxide ligands are very stable due to the conjugation with the aromatic system⁵⁹, consequently their Ln(III) complexes are very stable as well. The stability constants of picolinic acid N-oxide increase from La(III) to Lu(III)⁶⁶, which is probably due to the decreasing size La→Lu. Picolinate ion is hundred times more basic than corresponding N-oxide, as shown by $pK_a$: 4.58×10⁻⁶ for picolinic acid and 4.85×10⁻⁴
for N-oxide. This indicates that complexes with picolinic acid are considerably more stable. Moreover, picolinites form more stable five-membered ring upon complexation vs. six-membered ring in case of N-oxides.\textsuperscript{66}

Uranyl nitrate easily forms complexes with methylpyridine-N-oxide isomers. Using the x-ray powder diffraction it was determined that the general formula is $\text{UO}_2(\text{NO}_3)_2 \cdot 2\text{L}$, where L is a N-oxide ligand. Complexes were prepared with 1:2 metal to ligand ratio, as a result only two nitrate ions have been replaced by N-oxide ligand.\textsuperscript{67} Coordination sphere of the metal ion is completely filled by the terpyridine N-oxide ligands in the complexes with Eu(III). The addition of the three equivalents of the terpyridine-1-oxide resulted in the nine coordinate trigonal tricapped prismatic geometry, while the addition of the terpyridine-1,1,1-trisoxide in the 8 coordinate geometry with one non binding N-oxide donor. The coordination geometry around the Eu(III) is not certain.\textsuperscript{68} From this data it can be inferred that most stable is the mono-N-oxide chelate, and in fact, the enthalpy of formation with Zn(II), Hg(II) and Cd(II) confirms that pyridine N-oxide is a better ligand for metal complexation than bipyridinedioxide.\textsuperscript{69}

N-oxide derivatives are commercially available and can be readily synthesized in the lab. One of these derivatives is a picolinic acid N-oxide. The similarities of the binding site between the N-oxide and CMPO led to the idea that the former should be interesting in its extraction capabilities.

\section*{Results and Discussion}

\section*{Preparation of Tripodal N-oxide Ligand}

Preparation of the ligand was attempted by reacting freshly prepared 2-picolinyl chloride with the triphenoxymethane platform 1-6 and then oxidizing pyridine nitrogen to N-oxide with $m$-chloroperoxybenzoic acid ($m$CPBA). But the last step, oxidation of the
ligand precursor, would not go to completion despite multiple attempts. Inability of mCPBA to oxidize tris-picolinic acid to tris-N-oxide was determined by the absence of the chemical shift of the N-H peak, which was supposed to shift downfield due to changes of the electronic character of the ligand. Instead it appeared at 9.87 ppm, as in the unoxidized product. Unlike in more flexible upperside preorganized ligands, steric hindrance of 1-6-7 could have prevented mCPBA from attacking N atom on the pyridine ring.

Alternatively, preparation of the ligand 1-6-7 was accomplished by a coupling reaction between platform 1-6 and picolinic acid N-oxide 7. Reaction was carried out similar to the coupling of pyridine-2,6-dicarboxamides, but with some modifications. Dichloromethane was used as a solvent instead of N,N-dimethylformamide, and when reflux was complete, the mixture was washed with 1 M HCl, 1 M NaOH and brine. Product was obtained by adding pentane after removing the solvent and drying the ligand under vacuum.

**Extraction Performance**

Extraction performance of ligand 1-6-7 was evaluated similarly to DPA and DPA-S extractants (Figure 4-1). The ligand showed very low affinity towards lanthanides with
Figure 2. Metal extraction percentages (%E) for ligand 1-6-7 using 10:1 ligand to metal ratio with 10⁻³ M ligand and 10⁻⁴ M metal nitrate; and 10:10:1 COSAN to ligand to metal ratio with 10⁻³ M COSAN, 10⁻³ M ligand and 10⁻² M metal nitrate in dichloroethane.

Table 4-3. Percent extraction (%E), percent error (% error) and distribution ratios (D) for extraction experiments with ligand 1-6-7

<table>
<thead>
<tr>
<th></th>
<th>1-6-7</th>
<th></th>
<th>1-6-7 with COSAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>%E</td>
<td>% error</td>
<td>D</td>
<td>%E</td>
</tr>
<tr>
<td>La</td>
<td>5.18</td>
<td>2.25</td>
<td>0.05</td>
</tr>
<tr>
<td>Ce</td>
<td>5.04</td>
<td>2.04</td>
<td>0.05</td>
</tr>
<tr>
<td>Pr</td>
<td>6.21</td>
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</tr>
<tr>
<td>Nd</td>
<td>3.79</td>
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<td>0.04</td>
</tr>
<tr>
<td>Eu</td>
<td>3.05</td>
<td>2.18</td>
<td>0.03</td>
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<td>Gd</td>
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</tr>
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<td>Tb</td>
<td>6.55</td>
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<td>0.07</td>
</tr>
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<td>8.66</td>
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<tr>
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<td>0.10</td>
</tr>
<tr>
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<td>0.11</td>
</tr>
<tr>
<td>Yb</td>
<td>9.21</td>
<td>0.43</td>
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The extractions were performed in 10:1 ligand to metal ratio using 10⁻⁴ M metal nitrate in 1 M nitric acid and 10⁻³ M ligand in dichloromethane. The extraction involving COSAN were performed in 10:10:1 COSAN to ligand to metal ratio using 10⁻³ M metal nitrate in 1 M nitric acid, 10⁻⁴ M ligand and 10⁻³ M COSAN in dichloroethane.

10:1 ligand to metal ratio in dichloromethane. Preorganization of picolinic acid N-oxide fragment on the upper side platforms similar to 2-2 and 3-2 have already been
accomplished, and resulted in very poor extraction results as well. The highest %E did not exceed 11± 3%.

In order to determine if low extractability is due to low solubility of the extracted complex, the extractions were repeated in the presence of COSAN counterion with 10:10:1 COSAN to ligand to metal ratio. The %E values did not improve which could mean that absence of extractability is due to low thermodynamic stability of the metal-ligand complex. Similar extractions with COSAN with upper side preorganized ligands did not improve %E as well. The change of solvent from dichloroethane to 2-nitrophenyl octyl ether and variation of COSAN to ligand to metal ratio was also unsuccessful.

**Conclusions**

Tripodal picolinic acid N-oxide was unable to extract Ln(III) metal ions from 1 M HNO$_3$. The extraction experiment with COSAN counterion did not improve the extraction ability, suggesting that solubility of the ligand is not a limiting factor. Protonation of the N-oxide can prevent metal binding, but as reported, N-oxides are stable in highly acidic environment, besides, Coulombic attraction of Ln$^{3+}$ will prevail over H$^+$. The ability of N-oxides to complex lanthanides has been confirmed with multiple examples, including preorganized platforms. Since N-oxides are bidentate ligands, low %E can be attributed to the lack of TTP geometry around the metal center, despite strong interaction between hard donor oxygen atoms and Ln(III). In addition, tripodal platform also restricts the ability of the chelate to wrap around the metal, which can hinder metal extraction even further.
Experimental Section

General Considerations

All reagents were used as received unless otherwise mentioned. Lanthanide salts were purchased from Aldrich. Metal solutions in 1M HNO₃ were prepared form 18 MΩ Millipore deionized water, TraceMetal-grade HNO₃ (Fisher Scientific), and HPLC-grade organic solvents. Absorbance of the extracted phase was measured on a Varian Cary 50 UV-vis spectrophotometer. All of the ¹H and ¹³C NMR spectra were recorded on a Varian Gemini-300 and Mercury-300 spectrometer at 299.95 MHz.

Metal Ion Extractions

The extraction of lanthanides, following a previously reported procedure, was performed using dichloromethane as a solvent for the organic phase.⁹,²⁴,⁴⁰ The extractability of each cation was calculated as \( \% E = 100/(A₁ - A)/(A₁ - A₀) \), \( \lambda_{\text{Ln(III)}} = 665 \) nm. Distribution values were determined as \( D = [M_{\text{org}}]/[M_{\text{aq}}] \). Extraction procedure was the same as in case of DPA derivatives. Phases were contacted over 16 hours, extractions were performed in triplicates on a series of eleven lanthanides with 10:1 ligand to metal ratio. After the vials were removed from the rotator the layers were allowed to separate during one hour. Extraction experiment with COSAN was performed with 10:10:1 COSAN to ligand to metal ratio: 1×10⁻³ M ligand in 1×10⁻³ M HCOSAN-dichloroethane solution and equilibrating it with 10⁻⁴ M Ln(III) in 1M HNO₃.

Ligand Synthesis

Preparation of 2,2',2''-(5,5',5''-methanetriyltris(4-methoxy-3-methylbenzene-5,1-diyl))tris(azanediyld)tris(oxomethylene)tripyridine 1-oxide 1-6-7.

The procedure for the preparation of 1-6-7 was adopted from the synthesis of tris-diglycolamides⁸,⁴¹. To a solution of 0.3 g (0.71 mmol) 5,5',5''-methanetriyltris(4-methoxy-
3-methylaniline) 1-6 in 20.0 ml of DCM, 0.74 ml (4.74 mmol) of N,N-diisopropylethylamine, 1.35 g of PyBOP (2.61 mmol) and 0.33 g of picolinic acid N-oxide 7 (2.37 mmol) were added. The mixture was stirred overnight under nitrogen followed, washed with 1M NaOH and brine and then dried with MgSO₄. After the solvent was removed in vacuo, n-pentane was added and the solid product was collected by filtration to give 85% yield (0.49 g). \(^1\)H NMR (CDCl₃): δ ppm: 2.33 (s, 9 H, Ar-CH₃), 3.58 (s, 9 H, Ar-OC₃H₃), 6.57 (s, 1 H, C-H), 6.83 (br. s., Ar-H), 7.35 (td, J=6.87, 2.12 Hz, 3 H, Py-H), 7.40 - 7.49 (m, 3 H, Py-H), 7.83 (br. s., 3 H, Ar-H), 8.21 (d, J=6.23 Hz, 3 H, Py-H) 8.47 (dd, J=8.07, 2.12 Hz, 3 H, Py-H), 13.16 (s, 3 H, N-H). \(^{13}\)C NMR (CDCl₃): δ ppm 16.66, 38.10, 60.07 (aliphatic); 120.76, 123.20, 127.12, 127.26, 128.99, 131.71, 132.83, 137.26, 140.27, 141.01, 153.62 (aromatic); 156.88 (C=O). HR ESI MS [M+H]^+ = 785.2918, [M+Na]^+ = 807.2766. Theoretical m/z [M+H]^+ = 785.2930, [M+Na]^+ = 807.2749.
APPENDIX
NMR SPECTRA OF THE C₃-LIGANDS
$^{13}$C $5,5',5''$-methanetriyltris(4-methoxy-3-methylaniline) 1-6
$^1$H $N^2,N^2',N^2''-(5,5',5''-\text{methanetriyltris}(4\text{-methoxy-3-methylbenzene-5,1-diyl}))\text{tris}(N^6,N^6\text{-diethylpyridine-2,6-dicarboxamide})$ 1-6-4

Chemical Shift (ppm)

- 9.62
- 8.28
- 8.06
- 7.97
- 7.27
- 6.58
- 6.51
- 6.57
- 3.40
- 3.37
- 3.23
- 3.21
- 2.37
- 1.85
- 1.12
- 0.88
- 1.04
- 1.06
- 1.09

Normalized Intensity

- 1.0
- 0.9
- 0.8
- 0.7
- 0.6
- 0.5
- 0.4
- 0.3
- 0.2
- 0.1
- 0.0

Chemical Shift (ppm)
$^{13}$C $N^2,N^2',N^{2''}-(5,5',5''$-methanetriyltris(4-methoxy-3-methylbenzene-5,1-diyl))tris($N^6,N^6$-diethylpyridine-2,6-dicarboxamide) 1-6-4
$^1$H $N^2,N^2',N^{2''}-(5,5',5''$-methanetriyltris(4-methoxy-3-methylbenzene-5,1-diyl))tris($N^6,N^6$-diisopropylpyridine-2,6-dicarboxamide) 1-6-5
\(^{13}\text{C}\) \(N^2,N^2,N^2\)\text{-}(5,5',5''\)-methanetriyltris(4-methoxy-3-methylbenzene-5,1-diyl))tris(\(N^6,N^6\)-diisopropylpyridine-2,6-dicarboxamide) 1-6-5
$^1$H $N^2,N^2',N^2''-(2,2',2''-(6,6',6''-methanetriyl)tris(4-tert-butyl-2-methylbenzene-6,1-diyl)tris(oxy))tris(ethane-2,1-diyl))tris(N^6,N^6'-diethylpyridine-2,6-dicarboxamide) \textbf{2-2-4}$

![Chemical Shift Graph](2-2-4_10-06-09.esp)
$^{13}$C $N^2,N^2',N^2''-(2,2',2''-(6,6',6''-\text{methanetriyltris(4-tert-butyl-2-methylbenzene-6,1-diyl)tris(oxy))tris(ethane-2,1-diyl))tris(N^6,N^6'-\text{diethylpyridine-2,6-dicarboxamide})$ 2-2-4

13C_2-2-4_07-31.esp

CHLOROFORM-d

Chemical Shift (ppm)
$^{1}H N^{2}, N^{2'}, N^{2''}(3,3',3''-(6,6',6''-methanetriyltris(4-tert-butyl-2-methylbenzene-6,1-diyl))tris(oxy))tris(propane-3,1-diyl))tris(N^{6}, N^{6'}-diethylpyridine-2,6-dicarboxamide) 3-2-4$
$^1$H $N^2,N^2',N^2''-(5,5',5''-\text{methanetriyltris}(4\text{-methoxy}-3\text{-methylbenzene}-5,1\text{-diyl})\text{tris}(N^6,N^6\text{-diisopropylpyridine}-2,6\text{-bis(carbothioamide)})$ **1-6-5-S**

1-6-5-S-DPA-cryst

[Chemical Shift Graph]

- Chemical Shift (ppm): 11.55, 8.68, 8.65, 8.42, 7.87, 7.85, 7.82, 7.57, 7.27, 6.89, 6.52, 3.90, 3.87, 3.85, 3.67, 2.38, 1.61, 1.07, -1.05
- Normalized Intensity
$^{13}$C $N_2,N_2',N_2''$-(5,5',5''-methanetriyltris(4-methoxy-3-methylbenzene-5,1-diyl))tris($N_6,N_6'$-diisopropylpyridine-2,6-bis(carbothioamide)) 1-6-5-S
$^1$H $2,2',2''-(5,5',5''$-methanetriyltris(4-methoxy-3-methylbenzene-5,1-diyl))tris(azanediyl)tris(oxomethylene)tripyridine 1-oxide 1-6-7
$^{13}$C $2,2',2''-(5,5',5''$-methanetriyltris(4-methoxy-3-methylbenzene-5,1-diyl))tris(azanediyl)tris(oxomethylene)tripyridine 1-oxide 1-6-7
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BIOGRAPHICAL SKETCH

Anna Vladimirovna Sberegaeva was born in St. Petersburg, Russia in 1984. She graduated from Herzen State University with a specialist degree in Chemistry in 2006. During her undergraduate studies she was working on a collaborative project with the University of Northern Iowa and Herzen State University together with Dr. Bartak and Dr. Timonov. Upon graduation she came to the University of Florida and was working in Dr. Mike Scotts research group until 2009. Anna received her MS degree in chemistry in 2009.