

Development of Highly Selective Ligands for Separations of Actinides from Lanthanides in the Nuclear Fuel Cycle

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Received 9 April 2011

We dedicate this paper to the memory of Dr. Charles Madic.

Abstract: This account summarizes recent work by us and others on the development of ligands for the separation of actinides from lanthanides contained in nuclear waste streams in the context of a future European strategy for nuclear waste management. The current status of actinide/lanthanide separations worldwide is briefly discussed, and the synthesis, development, and testing of different classes of heterocyclic soft *N*- and *S*-donor ligands in Europe over the last 20 years is presented. This work has led to the current benchmark ligand that displays many of the desirable qualities for industrial use. The improvement of radiolytic stability through ligand design is also discussed.

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Key words: heterocycles, ligands, actinides, solvent extraction, lanthanides

1 Introduction and Background

The generation of electricity through nuclear power is becoming increasingly important in order to meet future energy demands while minimizing the production of greenhouse gases.¹ As a result, the inventory of nuclear waste worldwide and thus its environmental burden will continue to increase.² However, an effective strategy for the improved safe long-term management and disposal of the waste still remains to be established.

The spent nuclear fuel produced by a typical light water reactor is composed of uranium (U) and short-lived fission products such as lanthanides (>98.5 wt%), which do not pose a long-term hazard, together with plutonium (Pu) and the minor actinides americium (Am), curium (Cm),

and neptunium (Np) (approx. 1 wt%), which are highly radiotoxic. The PUREX (Plutonium and URanium EXtraction) process involving tributyl phosphate (**1**) (Figure 1) is currently used to separate the Pu from the remaining waste, enabling its recycling and reuse as MOX (mixed oxide) fuel in nuclear reactors.³ The remaining high-level liquid waste (PUREX raffinate) still contains the minor actinides. The long-term radioactivity ($t_{1/2} = 10^3$ – 10^6 years) of these elements presents a serious environmental and economic problem for the safe management and storage of the waste and necessitates that it be isolated from the biosphere in perpetuity.

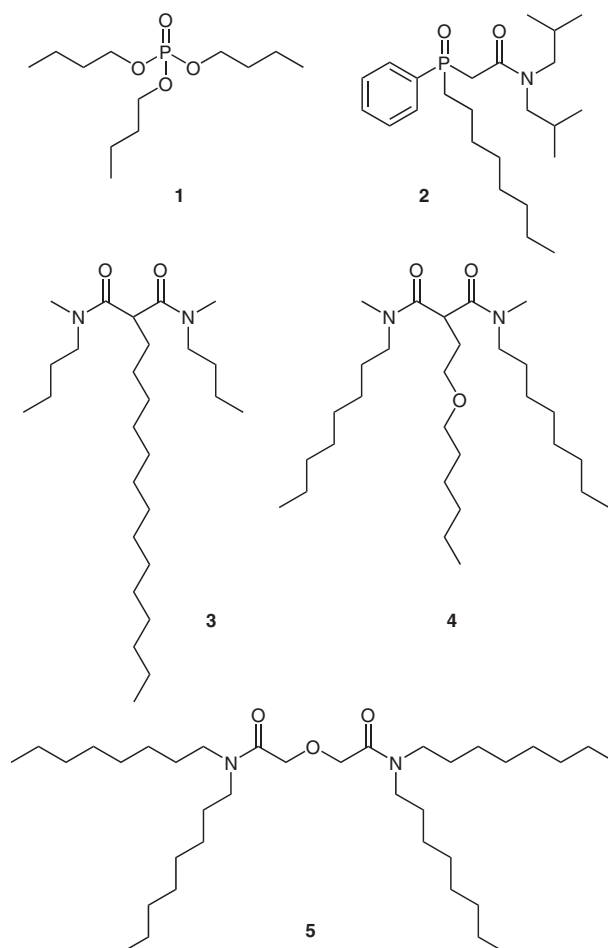


Figure 1 Structures of ligands used in the PUREX, TRUEX, and DIAMEX processes

SYNLETT 2011, No. 18, pp 2609–2632

Advanced online publication: 25.10.2011

DOI: 10.1055/s-0030-1289557; Art ID: A59611ST

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One possible strategy to reduce the radiotoxicity of the waste involves neutron bombardment (transmutation) of the minor actinides to give shorter-lived ($t_{1/2} = 10^1$ years) or stable elements.⁴ However, the lanthanides have high neutron capture cross sections and absorb the neutrons in preference to the transmutable actinides. It is, therefore, necessary to first separate (partition) the actinides from the bulk of the lanthanides prior to their transmutation. This strategy, known as 'partitioning and transmutation',⁵ is a promising alternative to long-term deep geological disposal of the high-level waste.

In recent decades, there has been intensive research worldwide on the development of solvent extraction processes for the partitioning of actinides from lanthanides as part of a future strategy for the reprocessing of spent nuclear fuel.⁶ Within Europe, this research has led to the development of two proposed sequential processes. In the first process, both actinides and lanthanides are co-extracted from PUREX raffinate by a nonselective, diamide-based ligand. This is known as the DIAMEX (DIAMide EXtraction) process.⁷ In the second process, known as the SANEX (Selective ActiNide EXtraction)

process, the intention is to selectively extract and separate the minor actinides from the lanthanides. Currently, the TRUEX (TRansUranium EXtraction) process, which employs [(*N,N*-diisobutylcarbamoyl)methyl](octyl)phenylphosphine oxide (CMPO, **2**) (Figure 1) as the principal extractant, is used in the United States⁸ to recover the actinides and lanthanides from high-level waste solutions, but no process is currently used worldwide for the actinide/lanthanide group separation.

Within the framework of several European Union funded research projects, a number of substituted diamide ligands have been developed for the DIAMEX process.⁹ Among these, *N,N'*-dibutyl-*N,N'*-dimethyltetradecylmalonamide (**3**)¹⁰ and *N,N'*-dimethyl-*N,N'*-dioctyl[(hexyloxy)ethyl]malonamide (DMDOHEMA, **4**)¹¹ have shown the most promising results in extraction tests on genuine fuel solutions. More recently, *N,N,N',N'*-tetraoctyldiglycolamide (TODGA, **5**) (Figure 1) has shown superior performance in comparison with **3** or **4** when tested on PUREX raffinate, and this extractant is currently the preferred ligand for the DIAMEX process.¹²

Biographical Sketches



Frank W. Lewis was born in Dublin, Ireland, in 1976. He graduated with a B.A. in chemistry from Trinity College Dublin in 1998. After a period of self-employment, he commenced graduate studies with Professor David Grayson at Trinity

College Dublin where he obtained his Ph.D. in organic chemistry in 2008. He is currently a postdoctoral fellow in the group of Professor Laurence Harwood at the University of Reading, UK, where he is working on the design and synthesis of

ligands for the selective extraction of minor actinides from nuclear waste solutions. His research interests are asymmetric synthesis, sulfone chemistry, and ligand design.



Michael J. Hudson studied chemistry at University College London where he obtained his Ph.D. in 1965. He has published over 100 refereed papers on separation processes that involve precious metals, actinides and

base metals. He was awarded the D.Sc. from the University of London in 2000. He has received extensive financial support for the partitioning of minor actinides from the lanthanide elements. He was responsible

for the design and development of many heterocyclic molecules, including the BTBP molecules, which are discussed later in this review.



Laurence M. Harwood is the Professor of Organic Chemistry at the University of Reading. He studied chemistry at Manchester University where he obtained his Ph.D. in 1978. After two years working for Professor Marc Julia at the

École Normale Supérieure in Paris as a Royal Society Postdoctoral Fellow, he returned to Manchester for his first academic position before moving to Oxford University and Merton College in 1983. He moved to his current position in 1995 and

has been the UK Regional Editor for *Synlett* since 2001. His research interests lie in applications of synthetic methodology to a wide range of natural and unnatural targets.

In the SANEX process, the separation of actinides from lanthanides is much more challenging because of the chemically similar behavior of the two groups of elements (identical oxidation states, similar ionic radii owing to lanthanide/actinide contractions).¹³ However, there is a more covalent contribution to metal–ligand bonding with the actinides than with the lanthanides. Consequently, ligands with softer donor atoms (e.g., N and S) that favor complexation with the 5f orbitals of the actinides have been the focus of research in order to exploit this difference between the coordination chemistries of the actinides and lanthanides. In the United States, the TALSPEAK (Trivalent Actinide - Lanthanide Separation by Phosphorus reagent Extraction from Aqueous Komplexes) process has been proposed to carry out this separation.¹⁴

Ligands suitable for the separation of actinides from lanthanides in a SANEX process must obey a demanding set of criteria.¹⁵ They should have a sufficiently high solubility in the organic diluent used for the extraction. The extracted species must also have good solubility in the organic phase to prevent third phase formation or precipitation. The ligand must show a high enough selectivity for the actinides so that the separation can be carried out in a relatively small number of extraction stages. It is also desirable that the affinity for the actinides is not so high that the back-extraction (stripping) of the metal from the extracted complexes and the subsequent recycling of the organic phase cannot take place. The ligand must show acceptable resistance towards both acidic hydrolysis and radiolysis, and any degradation products that form must not interfere with the extraction. The ligand should be able to extract from highly acidic (up to 4 M HNO₃) solutions. It is also desirable that the ligand is composed of only carbon, hydrogen, oxygen, and nitrogen (CHON principle) so that the ligand or its degradation products can be completely incinerated at the end of its useful life, thereby avoiding secondary waste generation. Finally, the ligand must be as cheap and easy to synthesize as possible so that large-scale commercial production is feasible.

In solvent extraction experiments, ²⁴¹Am(III) and ¹⁵²Eu(III) radioisotopes are typically used as representatives for the actinides and lanthanides, respectively. The effectiveness of a ligand in extracting a metal (M) is quantified by the distribution ratio (D_M), which is the equilibrium ratio between the metal concentration in the organic and in the aqueous phase. The separation factor for Am over Eu ($SF_{Am/Eu}$) is the ratio of the D values for Am and Eu and is thus a measure of the selectivity of a ligand for the actinides over the lanthanides. Thus, the optimum ligand will have a $D_{Am} > 1$ and an $SF_{Am/Eu}$ as large as possible.

A large number of potential SANEX ligands have been developed in recent decades.¹⁶ In this account, we review the *N*- and *S*-donor ligands for the SANEX process that have been developed within the framework of several European Union funded research programs and which show the most promising properties for actinide (An)/lanthanide (Ln) separations. The harder *O*-donor ligands,

which are generally non-selective, are thus outside the scope of this review.

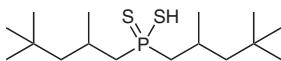
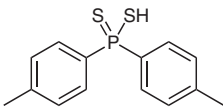
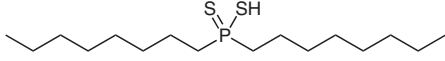
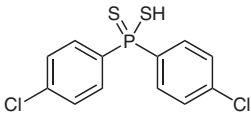
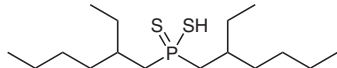
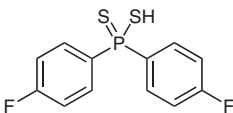
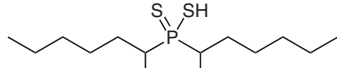
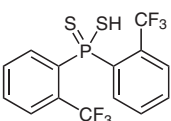
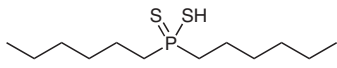
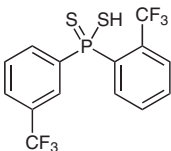
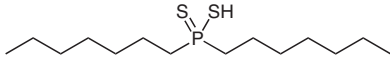
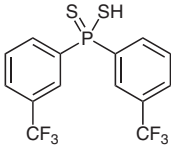
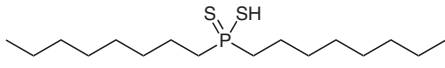
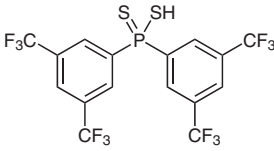
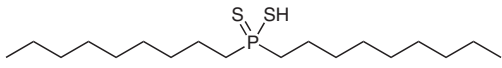
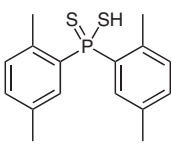
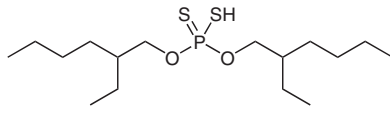
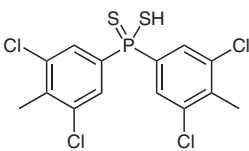
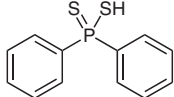
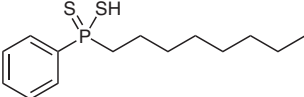
2 Dithiophosphinic Acids

The bidentate, *S*-donor dithiophosphinic acids were one of the first classes of reagent to show very high selectivities for An(III) over Ln(III). Dithiophosphinic acids studied for their ability to separate An(III) from Ln(III) are shown in Table 1. It was shown in early studies by Zhu that Cyanex 301, a commercial reagent composed mainly (~80%) of bis(2,4,4-trimethylpentyl)dithiophosphinic acid (**6**), efficiently separated Am(III) from Ln(III) with very high selectivities. The selectivity of the extraction increased when the reagent was fully purified ($SF_{Am/Eu} > 4000$, average $SF_{Am/Ln} > 2300$).¹⁷ Both the extraction efficiency and selectivity were enhanced in the presence of several *O*-donor synergists that formed mixed metal complexes with **6**.¹⁸ In synergistic combination with the softer *N*-donor ligands 2,2'-bipyridine and 1,10-phenanthroline, the selectivity was further enhanced, resulting in one of the highest reported separation factors to date ($SF_{Am/Eu} > 40000$).¹⁹

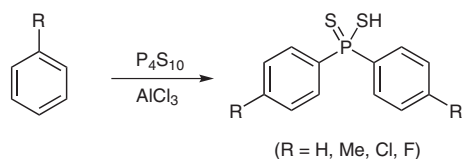
Promising results were also observed in the extraction of An(III) and Ln(III) from acetic acid/ammonium acetate buffered solutions that would result from a preceding TRUEX separation step.²⁰ In addition, the successful separation of An(III) from Ln(III) by purified bis(2,4,4-trimethylpentyl)dithiophosphinic acid (**6**) immobilized on silica resins,²¹ enclosed in biopolymer microcapsules,²² or in supported liquid membranes,²³ has been demonstrated. In a laboratory-scale countercurrent extraction test, >99.998% of Am(III) was extracted and separated from macro amounts of Ln(III) using purified **6** and tributyl phosphate.²⁴ Unfortunately, ligand **6** can only extract from nitric acid (HNO₃) solutions of relatively low acidity (pH > 2.5) owing to the nondissociation/oxidative degradation of the extractant at low pH. Furthermore, ligand **6** was found to decompose to its corresponding monothio-phosphinic acid and phosphinic acids on exposure to 700 kGy of gamma radiation, with deleterious effects on the extraction performance and selectivity.²⁵

To address these shortcomings, a series of more-acidic aromatic dithiophosphinic acids were developed by Modolo and co-workers. Compounds **14–17** were synthesized by the treatment of phosphorus pentasulfide with aluminum trichloride in the presence of an aromatic hydrocarbon (Scheme 1). The ligands efficiently extracted Am(III) and Eu(III) into toluene from 0.1–1 M HNO₃ in synergistic combination with tributyl phosphate or a trialkylphosphine oxide, with the best results being observed for bis(4-chlorophenyl)dithiophosphinic acid (**16**).²⁶ No extraction occurred with the ligands alone in the absence of a synergist. The dependence of the distribution ratios for An(III) on extractant concentration indicated that the dithiophosphinic acids extract An(III) as 1:3 complexes. The aromatic dithiophosphinic acids were also more resistant to radiolysis than Cyanex 301 composed of **6**. Only minor

Table 1 Dithiophosphinic Acids Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides

Ligand structure	Ref.	Ligand structure	Ref.
 6	17–25,35	 15	26b,27,33
 7	33	 16	26–31,33,34
 8	33	 17	26a,27
 9	33	 18	32
 10	33	 19	32b
 11	33	 20	32b
 7	33	 21	32a
 12	33	 22	33
 13	33	 23	33
 14	26a,b,27,33,35	 24	33

(<5%) decomposition was observed after exposure to 1000 kGy of gamma radiation, whereas >80% decomposition of Cyanex 301 compound **6** occurred under the same conditions.²⁷ However, complete oxidative degradation of the ligands occurred in contact with strongly acidic (>2 M) HNO₃ solution over 100 days.²⁸



Scheme 1 Synthesis of aromatic dithiophosphinic acids

The synergistic mixture of bis(4-chlorophenyl)dithiophosphinic acid (**16**) and tris(2-ethylhexyl) phosphate extracted Am(III) and Cm(III) from the lanthanides with very high separation factors ($SF_{Am/Ln} > 3000$). Furthermore, an Am(III)/Cm(III) separation factor of >8 was observed, suggesting that the system could be used for the challenging separation of Am(III) from Cm(III).²⁹ In a subsequent laboratory-scale separation process using centrifugal contactors, this synergistic combination selectively extracted 99.8% Am(III) from a mixture of Am(III), Cm(III), Cf(III), and Eu(III), with only 0.47% Cm(III) being extracted into the organic phase.³⁰

It has been shown that a donor–acceptor mechanism of extraction operates to promote the extraction of Am(III) by synergistic mixtures of dithiophosphinic acids and neutral *O*-donor ligands.³¹ Strong *O*-donor ligands, such as trialkylphosphine oxides, tend to strengthen the metal–sulfur bonds and increase D_{Am} , whereas weaker *O*-donor ligands, such as triaryl phosphates, tend to weaken the metal–sulfur bonds and decrease D_{Am} . For those synergists giving high Am/Eu separation factors (trialkyl phosphates), an antagonistic effect was observed for Eu(III) complex formation, but not for Am(III) complex formation.

More recently, bis[(trifluoromethyl)phenyl]dithiophosphinic acids **18–20** were synthesized regioselectively by a multistep route and were evaluated in Am(III) and Eu(III) solvent extraction experiments to determine the effect of the location of the trifluoromethyl group on the extraction properties.³² The *ortho*-substituted ligands **18** and **19** showed unprecedented selectivity for Am(III) over Eu(III) ($SF_{Am/Eu} > 100000$), but the *meta*-disubstituted ligand **20** was far less selective ($SF_{Am/Eu} = \text{ca. } 20$), demonstrating that the location of the substituent played a key role in the extraction selectivity. In a related study on several alkyl- and aryl-substituted dithiophosphinic acids, the presence of electron-withdrawing groups on the aromatic rings in the aryl-substituted ligands increased the selectivity, but decreased the extraction ability.³³ For the alkyl-substituted ligands, branched alkyl chains increased the selectivity.

The origin of the high selectivity of synergistic mixtures of bis(4-chlorophenyl)dithiophosphinic acid (**16**) and neutral *O*-donor ligands for An(III) over Ln(III) was es-

tablished by extended X-ray absorption fine structure spectroscopy (EXAFS) and time-resolved laser-induced fluorescence spectroscopy (TRLFS).³⁴ The structures of the inner coordination spheres of the Cm(III) and Eu(III) complexes were different. While Cm(III) primarily bound to the sulfur atoms of the ligand in a bidentate fashion, Eu(III) preferentially bound to the oxygen atoms of the synergist, suggesting that a high number of covalent metal–sulfur bonds are responsible for the high selectivity. The primary role of the synergist appears to be co-complexation of the metal ions to form more-hydrophobic complexes. Molecular dynamics simulations show that the ligands and their Eu(III) complexes are surface active, but synergists such as tributyl phosphate also promote the extraction to the organic phase by aggregating at the interface where they lower its surface tension and promote the transfer of the complexes into the organic phase.³⁵

3 2,2':6',2''-Terpyridine (TERPY) and Related Ligands

The tridentate aromatic *N*-donor ligand 2,2':6',2''-terpyridine (TERPY, **25**) was one of the first *N*-donor ligands investigated for its ability to extract Am(III) from Eu(III) selectively. 2,2':6',2''-Terpyridine and its derivatives that were tested for their ability to separate Am(III) from Eu(III) are shown in Table 2. In synergistic combination with 2-bromodecanoic acid, which acts as a lipophilic anion source, TERPY selectively extracted Am(III) from weakly acidic aqueous solutions of up to 0.1 M HNO₃ into hydrogenated tetrapropene (TPH) with an $SF_{Am/Eu}$ of 7.2.^{36,37} However, the D value for Am(III) progressively decreased at higher acidities ($[HNO_3] > 0.1$ M) owing to protonation and subsequent dissolution of the ligand in the aqueous phase. No significant extraction of Am(III) or Eu(III) was observed using TERPY alone.

The more-hydrophobic derivatives 4'-octyl-2,2':6',2''-terpyridine (**26**) and 4,4',4''-tri-*tert*-butyl-2,2':6',2''-terpyridine (**27**) (Table 2) were then investigated. However, at comparable acidities the D values for Am(III) were substantially lower than for TERPY (**25**).³⁶ Although alkyl substitution was expected to increase the D values by improving the solubility of the extracted complex in the organic phase, it appeared to increase the basicity of the ligand so that protonation of the donor atoms competed effectively with metal ligation. Similar results were observed with phenyl-substituted derivatives **28**, **29**, and **31**, and pyrazine derivative **30**.³⁸ All the substituted ligands became protonated at higher acid concentrations and precipitation of the protonated ligands was observed in some cases.

In an effort to understand better the types of species that may be involved in the extraction, a series of complexes formed by TERPY (**25**) and the lanthanides were synthesized and structurally characterized.^{38,39} In most cases, neutral 1:1 species $[M(L)(NO_3)_3]$ ($L = \text{TERPY}$) were observed, although with neodymium, samarium, terbium, dysprosium, and holmium, complex ion pairs composed

of $[M(L)_2(NO_3)_2]^+$ cations and $[M(L)(NO_3)_4]^-$ anions were seen. However, under anhydrous conditions, 1:2 complexes of the formula $[M_2(L)_2]I$ were formed between TERPY (**25**) and MI_3 ($M = Ce, Nd, U$).⁴⁰ X-ray crystallographic analysis revealed shorter average metal–nitrogen distances in the U complex than in the cerium one, suggesting a possible π -backbonding interaction and thus greater covalency in the U(III) complex.

The structures of the mono- and diprotonated TERPY cations were determined by ab initio quantum mechanics calculations and by X-ray crystallographic analysis of the ion pairs formed between the diprotonated TERPY cation and nitratolanthanate ($[M(NO_3)_5]^{2-}$) anions of lanthanum and samarium.⁴¹ The isolation of these species in the solid state suggests that TERPY and its derivatives could extract the metals by an ion-pair mechanism as well as by simple solvation, particularly at high acidities.

4 2,4,6-Tri-2-pyridyl-1,3,5-triazine (TPTZ) and Related Ligands

The tridentate *N*-donor ligand 2,4,6-tri-2-pyridyl-1,3,5-triazine (TPTZ) and its derivatives are synthesized by cyclotrimerization of pyridine-2-carbonitriles under acidic, basic, or neutral conditions (Scheme 2).⁴²

Table 2 2,2':6',2''-Terpyridine and Related Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides

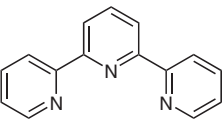
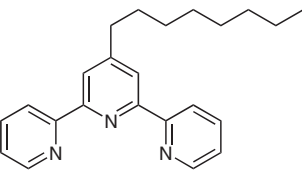
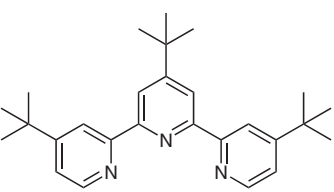
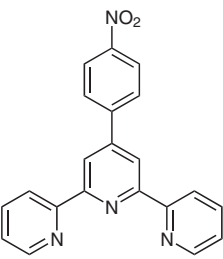
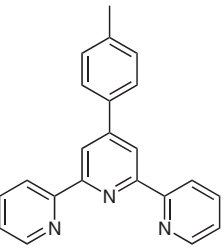
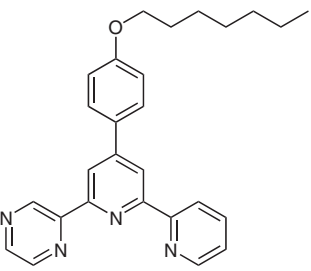
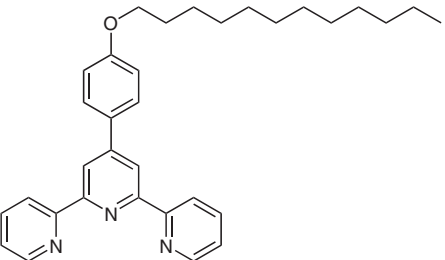
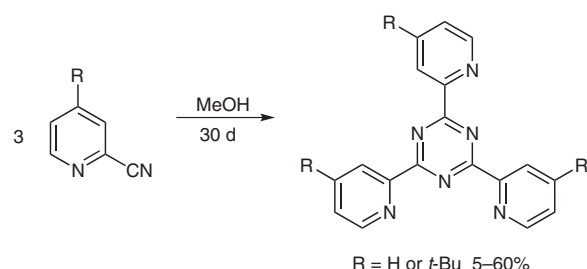
Ligand structure	Ref.
	36–41,46,73b,76b,78,109b
25	
	36
26	
	36
27	
	38
28	

Table 2 2,2':6',2''-Terpyridine and Related Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides (continued)

Ligand structure	Ref.
	38
29	
	38
30	
	38
31	



Scheme 2 Synthesis of 2,4,6-tri-2-pyridyl-1,3,5-triazine ligands

It was reasoned that replacing the central pyridine ring of TERPY (**25**) with a 1,3,5-triazine ring would reduce the basicity of the ligand and therefore lower the solubility of the protonated ligand in the aqueous phase at low pH. 2,4,6-Tri-2-pyridyl-1,3,5-triazine and related ligands that were tested for their ability to separate Am(III) from Eu(III) are shown in Table 3.

In solvent extraction experiments, TPTZ (**32**) performed slightly better than TERPY (**25**), and higher *D* values were observed for Am(III) when the ligand was used in combination with 2-bromodecanoic acid in TPH. 2,4,6-Tri-2-pyridyl-1,3,5-triazine (**32**) was also the first *N*-donor ligand to show an $SF_{Am/Eu}$ of >10. In contrast to the more-lipophilic derivatives of TERPY, the extraction was

further improved through the use of the more-lipophilic TPTZ derivative **33**, which gave slightly higher D_{Am} values than TPTZ (**32**) and an $SF_{\text{Am/Eu}}$ of 11.9.³⁶ Once again, however, the ligands were incapable of extracting the metals from solutions more acidic than 0.1 M HNO_3 .

Table 3 2,4,6-Tri-2-pyridyl-1,3,5-triazine and Related Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides

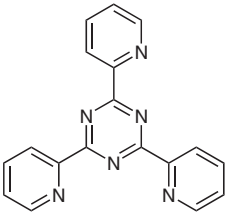
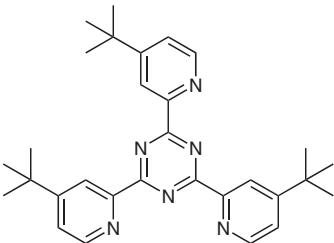
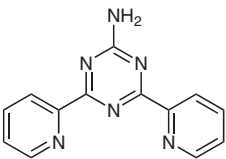
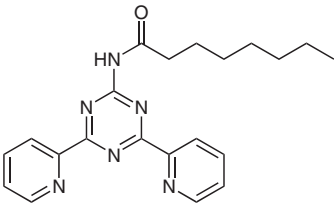
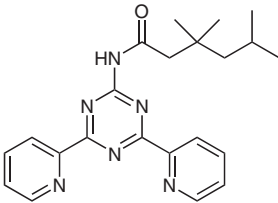
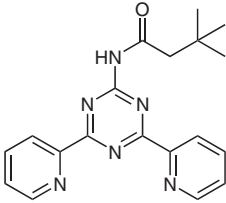
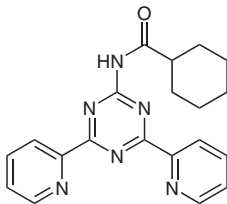
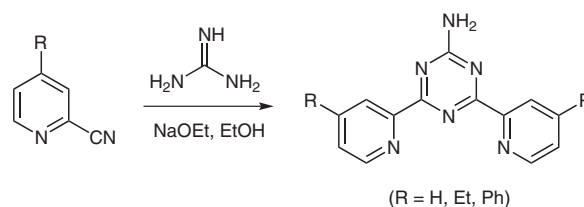
Ligand structure	Ref.
	36,37,42b,c,d,43b,76b,78,108
	36,42c,43a,46
	45,46,47,76b,78
	46
	46
	46

Table 3 2,4,6-Tri-2-pyridyl-1,3,5-triazine and Related Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides (continued)

Ligand structure	Ref.
	46

X-ray crystallographic structures of the 1:1 complexes formed between Ce(IV) and Sm(III) nitrates and 2,4,6-tris(4-*tert*-butyl-2-pyridyl)-1,3,5-triazine (**33**), and complexes in which the protonated ligand forms salts with a variety of anions have been obtained, illustrating the versatile coordination chemistry of this class of ligand.⁴³ With TPTZ (**32**), both 1:1 and 1:2 complexes with the trivalent lanthanides and actinides have been observed under different conditions.⁴⁴

The promising results obtained with TPTZ (**32**) and its derivatives led us to investigate the related ligand 4-amino-2,6-di-2-pyridyl-1,3,5-triazine (ADPTZ, **34**), which features the same tridentate coordination cavity as TPTZ (**32**), but is more easily functionalised to obtain more-hydrophobic derivatives. This and related ligands are synthesized by the treatment of pyridine-2-carbonitriles with guanidine in ethanolic sodium ethoxide (Scheme 3).^{42a}



Scheme 3 Synthesis of 4-amino-2,6-di-2-pyridyl-1,3,5-triazine ligands

The coordination chemistry of ADPTZ (**34**) with the trivalent lanthanides has been investigated.⁴⁵ X-ray crystallographic analysis revealed the formation of five structural types. In each case, the tridentate ligand formed 1:1 complexes and the remainder of the metal's inner coordination sphere was occupied by a combination of water molecules and nitrate ions. The structures appeared to be stabilized by intermolecular hydrogen bonding involving the free amino group.

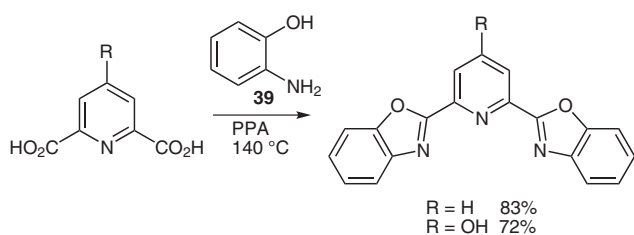
In Am(III)/Eu(III) solvent extraction experiments, ADPTZ (**34**) and its hydrophobic amide derivatives **35–38** (Table 3) gave results comparable to TPTZ (**32**) and its tri-*tert*-butyl-substituted derivative **33**.⁴⁶ Although relatively high D values for Am(III) were obtained in synergy with 2-bromodecanoic acid [e.g., $D_{\text{Am}} = 45$; organic phase: 0.02 M **34** and 1 M 2-bromodecanoic acid in TPH;

aqueous phase: 0.03 M HNO₃ with Am(III) and Eu(III) tracers], these values decreased rapidly as the concentration of HNO₃ increased. Distribution ratios for Am(III) of less than 1 were observed when the concentration of HNO₃ was 0.1 M. The selectivity (SF_{Am/Eu}) ranged between 6.5 and 12.

Amide derivatives **35–38** showed identical coordination chemistry towards the lanthanides as parent compound **34**, and crystallographic structures of the 1:1 complexes with Yb(III) have been obtained.⁴⁶ Complexation and microcalorimetry studies in water–methanol showed that the Am(III) complex of ADPTZ (**34**) was more stable than the lanthanide complexes by a factor of about 20, and this is driven primarily by a more exothermic enthalpy of complex formation.⁴⁷ This supports the view that the preference of the ligand for An(III) is due to a greater degree of covalency in the metal–ligand bonds than with Ln(III).

5 2,6-Bis(benzoxazol-2-yl)-4-dodecyloxy- pyridine (BODO) and Related Ligands

In searching for a new class of weakly basic ligand that could also separate An(III) from Ln(III), our attention was drawn to ligands related to 2,6-bis(benzimidazol-2-yl)pyridine whose synthesis takes place in polyphosphoric acid at 200–230 °C.⁴⁸ This stability towards strongly acidic conditions at high temperatures was considered very desirable for a future separation process. In addition, ligands based on the related 2,6-bis(benzoxazol-2-yl)pyridine and 2,6-bis(benzothiazol-2-yl)pyridine were expected to be less basic, as both benzoxazole and benzothiazole have pK_a values lower than benzimidazole. A typical procedure for the synthesis of 2,6-bis(benzoxazol-2-yl)pyridines is shown in Scheme 4.



Scheme 4 Synthesis of 2,6-bis(benzoxazol-2-yl)pyridine ligands

Thus, a range of hydrophobic tridentate pyridine ligands containing benzimidazole, benzoxazole, and benzothiazole rings (see Table 4) were synthesized and assessed for their ability to extract and separate An(III) from Ln(III).⁴⁹

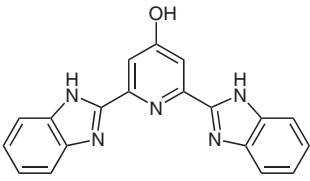
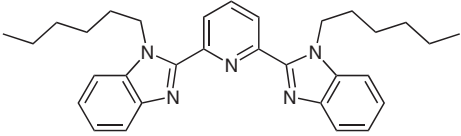
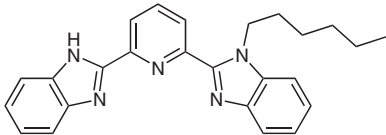
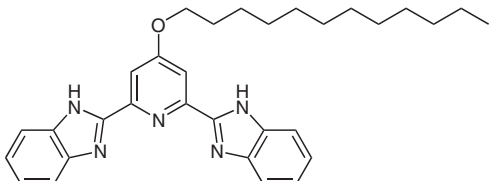
The most promising results were obtained with 2,6-bis(benzoxazol-2-yl)-4-dodecyloxy-*N*-dodecylpyridine (BODO, **42**) and its branched derivative **43** in combination with 2-bromodecanoic acid as a synergist. Relatively high separation factors were observed (SF_{Am/Eu} = 36–79 for **42**, 43–70 for **43**) and these values actually increased at higher acidities (up to 0.1 M HNO₃). This was the first time that an increase in SF_{Am/Eu} had been observed with increasing

HNO₃ concentration for *N*-donor ligands. The *D* values for Am(III) were greater for the branched ligand **43** than for BODO (**42**), but once again these values decreased as the concentration of HNO₃ increased further, and no significant extraction occurred at higher acidities.

Table 4 2,6-Bis(benzoxazol-2-yl)pyridine and Related Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides

Ligand structure	Ref.
	49
	49
	49,50
	49
	49
	49
	49,78

Table 4 2,6-Bis(benzoxazol-2-yl)pyridine and Related Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides (continued)

Ligand structure	Ref.
	49
	49
	49
	49

X-ray crystallographic studies of 2,6-bis(benzoxazol-2-yl)pyridine (**40**) showed that, as with other tridentate ligands based on TERPY and TPTZ, only 1:1 complex formation occurred with the trivalent lanthanide nitrates.⁴⁹

In further solvent extraction experiments with BODO (**42**), it was found that, at constant acidity, both D_{Am} and $SF_{Am/Eu}$ decreased as the concentration of either nitrate or perchlorate ions increased.⁵⁰ In addition, the ligand was not extracted into the aqueous phase when in contact with 2 M or 4 M HNO_3 solutions and could be recovered from the organic phase, demonstrating its resistance to protonation. The decrease in D_{Am} and Am/Eu selectivity with increasing nitrate concentration is most likely due to the inability of BODO (**40**) to compete with nitrate ions, which must be displaced from the metal by the ligand so that a hydrophobic extractable complex can form.

6 Podand Ligands

Encapsulating podand ligands are well known in coordination chemistry, and a series of polydentate podand *N*-donor ligands have been investigated for their ability to separate An(III) from Ln(III). The ligands investigated are presented in Table 5, and they are based on the parent tri-

podal ligands tris(2-pyridylmethyl)amine and tris(2-pyridyl)methanol and the tetrapodal ligand *N,N,N',N'*-tetrakis(2-pyridylmethyl)ethane-1,2-diamine (TPEN).

In solvent extraction experiments, tris(2-pyridylmethyl)amine (**51**) (1 mM in TPH) only weakly extracted Am(III) from HNO_3 solutions (D_{Am} = ca. 0.25 from ca. 0.01 M HNO_3) with low selectivity ($SF_{Am/Eu}$ < 2) in the presence of the synergist 2-bromodecanoic acid.⁵¹ The results with the softer, more-soluble ligand tris(pyrazin-2-ylmethyl)amine (**52**) were more promising (D_{Am} = 4.6, $SF_{Am/Eu}$ = 10.8 for 20 mM **52** in TPH), but no extraction occurred from more-acidic solutions (pH ≤ 1) owing to protonation of the ligands. More recently, chiral tris(2-pyridylmethyl)amine ligands **54–56** exhibited improved extraction performance at pH > 4.7 in nitrobenzene in the presence of 2-bromodecanoic acid.⁵² The best results were obtained with monomethyl compound (*R*)-**54** (D_{Am} = 52.3, $SF_{Am/Eu}$ = ca. 10) and dimethyl compound (*R,S*)-**56** (D_{Am} = 26.8, $SF_{Am/Eu}$ > 25).

A series of 1:1 complexes of tris(2-pyridylmethyl)amine (**51**) and tris(pyrazin-2-ylmethyl)amine (**52**) with the lanthanides have been isolated and characterized by X-ray crystallography.⁵¹ The structures show the ligand coordinates in a tetradentate capping mode with participation of the central podand nitrogen atom. A similar 1:1 complex was formed between tris(2-pyridylmethyl)amine (**51**) and $[U_3(THF)_4]$ under anhydrous conditions, but the related tripodal benzimidazoles **57** and **58** formed 1:2 complexes with U(III).⁵³ Solution NMR spectroscopic studies showed a greater stability of the 1:2 complexes of U(III) and La(III) with these ligands than with tris(2-pyridylmethyl)amine (**51**) owing to the presence of π - π stacking in the benzimidazole complexes. However, the successive formation of 1:1 and 1:2 complexes of tris(2-pyridylmethyl)amine (**51**) with the lanthanides was observed on addition of **51** to $Ln(OTf)_3$ and $[LnI_3(THF)_4]$ (OTf = triflate, THF = tetrahydrofuran) under rigorously anhydrous conditions, and the structures of the 1:2 complexes have been determined.⁵⁴

Analysis of lanthanide-induced 1H NMR spectroscopic shifts showed that tris(2-pyridylmethyl)amine (**51**) and its triamide derivative **53** have very similar formation constants, although the thermodynamic driving force for complex formation differs in each case. Whereas complexation of tris(2-pyridylmethyl)amine (**51**) is largely enthalpy driven, complexation with **53** is completely driven by entropy.⁵⁵ The additional ligating sites present in **53** displace more water molecules from the hydrated lanthanide ion during complex formation than **51**. The results of EXAFS on An(III) and Ln(III) complexes of tris(pyrazin-2-ylmethyl)amine (**52**) showed no obvious structural differences between the two sets of complexes,⁵⁶ although relatively short uranium(III)–nitrogen bond distances were observed, suggesting a higher degree of covalent character.

Table 5 Podand Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides

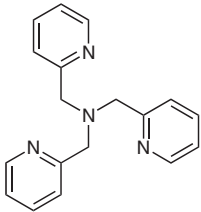
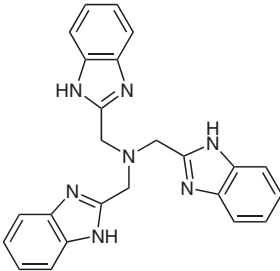
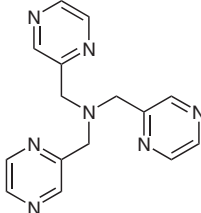
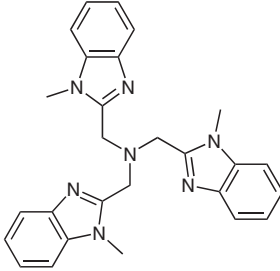
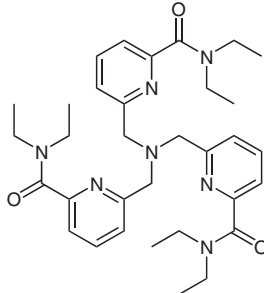
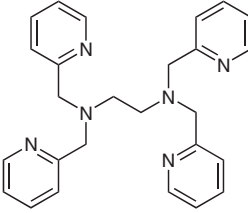
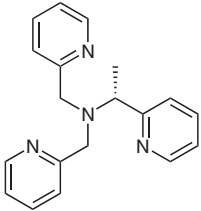
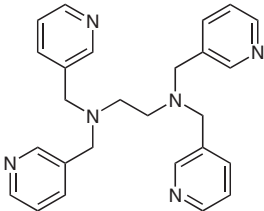
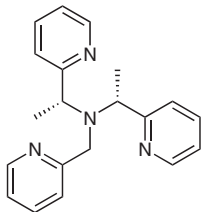
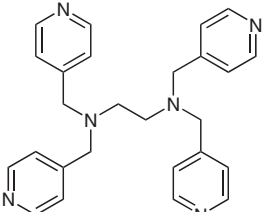
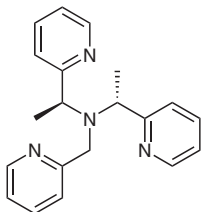
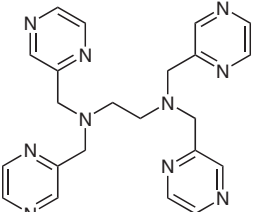
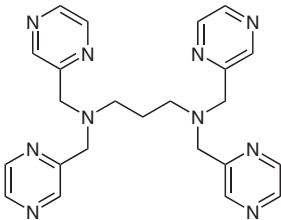
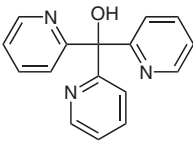
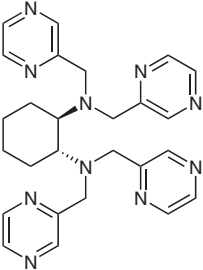
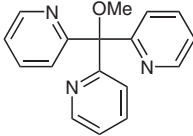
Ligand structure	Ref.	Ligand structure	Ref.
 <p>51</p>	51,53–55	 <p>57</p>	53
 <p>52</p>	51,56,59	 <p>58</p>	53
 <p>53</p>	55	 <p>59</p>	57,58
 <p>54</p>	52	 <p>60</p>	58
 <p>55</p>	52	 <p>61</p>	58
 <p>56</p>	52	 <p>62</p>	59

Table 5 Podand Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides (continued)

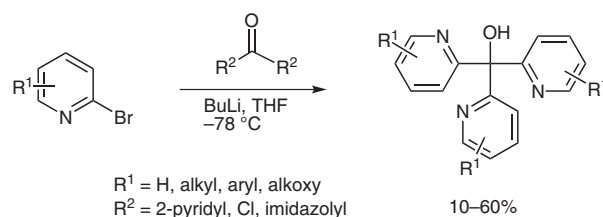
Ligand structure	Ref.	Ligand structure	Ref.
 <p>63</p>	59	 <p>65</p>	60a,61,62
 <p>64</p>	59	 <p>66</p>	61

The tetrapodal, hexadentate ligand *N,N,N',N'*-tetrakis(2-pyridylmethyl)ethane-1,2-diamine (TPEN, **59**) showed more promising results. In the absence of a synergist, solutions of **59** in nitrobenzene selectively extracted Am(III) over Eu(III) from ammonium nitrate solutions (pH 4) as 1:1 complexes with high efficiency and selectivity ($D_{\text{Am}} = \text{ca. } 100$, $\text{SF}_{\text{Am/Eu}} = \text{ca. } 100$ for 10 mM **59**). The results were broadly similar in the preferred diluent octan-1-ol in the presence of decanoic acid as a synergist, although the system did not extract from more-acidic (pH <4) aqueous solutions.⁵⁷ The related TPEN isomers **60** and **61** showed no significant extraction of either Am(III) or Eu(III), indicating the importance of the position of the *N*-donor atoms in the pyridine rings.⁵⁸

Pyrazine-containing analogues of TPEN (**59**) with different diamino spacers were then investigated. Excellent results were obtained in the extraction of Am(III) and Eu(III) into TPH solution using *N,N,N',N'*-tetrakis(pyrazin-2-ylmethyl)ethane-1,2-diamine (**62**) in the presence of 2-bromodecanoic acid ($D_{\text{Am}} = 45$, $\text{SF}_{\text{Am/Eu}} = 70$ for 0.1 M **62** from 0.03 M HNO_3). Interestingly, *N,N,N',N'*-tetrakis(pyrazin-2-ylmethyl)propane-1,3-diamine (**63**), which has a longer spacer and is thus more flexible, showed good extraction ability, but no selectivity ($\text{SF}_{\text{Am/Eu}} = 1.5\text{--}2.3$) under similar conditions.⁵⁹ The more-rigid ligand **64** bearing a *trans*-1,2-diaminocyclohexane spacer showed no significant extraction of either metal ion. The drastic difference in selectivity between **62** and **63** or **64** was explained by the different preferred conformations of the ligands as reflected by the X-ray structures of their 1:1 complexes with La(III).

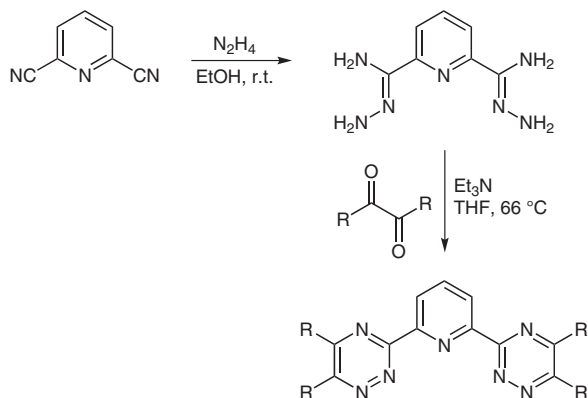
More recently, tris(2-pyridyl)methanol (**65**) and analogues have been studied as potential An(III)-selective extractants. These ligands are synthesized as shown in Scheme 5 by the addition of lithiated 2-bromopyridines to

phosgene, 1,1'-carbonyldiimidazole, or di-2-pyridyl ketone.⁶⁰ At pH >4.7, tris(2-pyridyl)methanol (**65**) selectively extracted Am(III) in synergistic combination with 2,4,6-trinitrophenol into nitrobenzene, 1,2-dichloroethane, or chloroform with $\text{SF}_{\text{Am/Eu}}$ values of 6.7–9.6. The corresponding methyl ether **66** showed similar selectivity, but the *D* values were about three orders of magnitude lower.⁶¹ The ligands extracted Am(III) as 1:3 complexes. Unusual homodinuclear 2:2 lanthanide complexes were obtained on treatment of tris(2-pyridyl)methanol (**65**) with $\text{La}(\text{OTf})_3 \cdot 3\text{H}_2\text{O}$. Each ligand coordinated in a tetradentate bridging mode with μ -oxo bridges formed by the hydroxy group of **65**.⁶²

**Scheme 5** Synthesis of tris(2-pyridyl)methanol ligands

7 2,6-Bis(1,2,4-triazin-3-yl)pyridine (BTP) and Related Ligands

Tridentate ligands based on 2,6-bis(1,2,4-triazin-3-yl)pyridine (BTP) were first synthesized by Case in 1971.⁶³ The BTP ligands are typically synthesized by the condensation reaction of pyridine-2,6-dicarbohydrazonamide with a 1,2-diketone (Scheme 6). Related 1,2,4-triazinyl-substituted pyridines have found use as synthetic precursors to functionalized oligopyridines.⁶⁴



Scheme 6 Synthesis of 2,6-bis(1,2,4-triazin-3-yl)pyridine ligands

In 1999, Kolarik et al. reported that alkyl-substituted BTPs and related 2,6-bis(1,2,4-triazolyl)pyridines separated Am(III) from Eu(III) with excellent selectivity ($SF_{Am/Eu} \leq 150$).⁶⁵ The BTP and related ligands that were screened for their ability to selectively extract Am(III) from Eu(III) are summarized in Table 6.

The extraction by the triazolyl-based ligands depended strongly on the diluent composition used, and a synergist (2-bromohexanoic acid) was required for efficient extractions. The related oxadiazolyl-based ligands performed similarly, but with lower extraction selectivity ($SF_{Am/Eu} \leq 23.3$).⁶⁶ In contrast, not only were the BTP ligands able to extract Am(III) selectively with very high efficiency ($1 \leq D_{Am} \leq 61$) in the absence of a lipophilic anion source [i.e., $Am(NO_3)_3$ was extracted], but they could also extract efficiently from solutions of high acidity ($[HNO_3] = 1\text{ M}$). This was a key breakthrough because up to this point, other heterocyclic *N*-donor ligands required synergists, such as 2-bromodecanoic acid, for efficient extractions and were unable to extract from highly acidic solutions that would be present in an industrial SANEX process.

Further solvent extraction studies were carried out on the most-promising BTPs: tetrapropyl- and tetraisopropyl-substituted compounds **70** and **71**, respectively (Table 6). The dependence of D_{Am} and D_{Eu} on the ligand concentrations showed that the metals were extracted as trisolvates of $[ML_3](NO_3)_3$ stoichiometry.⁶⁷ The rate of Am(III) extraction was determined by the rate of the complexation of the metal, and this increased linearly with the concentration of the BTP ligand, but decreased as the concentration of HNO_3 increased because of competing protonation of the ligand.⁶⁸ Initial attempts to isolate and structurally characterize the 1:3 complexes of the BTP ligands with the lanthanide nitrates were unsuccessful. Only complexes in which the cation contained one or two BTP ligands were obtained,⁶⁹ including an unusual 12-coordinate complex with Nd and Pr.⁷⁰ Structural and theoretical studies with the related bis(1,2,4-triazol-3-yl)pyridine ligands **79** and **80** showed that only complexes containing one ligand and one or more nitrates in the metal's inner coordination sphere were formed.⁷¹

Eventually, X-ray crystallographic structures of the 1:3 complexes of tetrapropyl-substituted BTP **70** with Sm(III), Tm(III), and Yb(III) nitrates were obtained and showed that the metal ions were completely enclosed by three ligands while the nitrates were displaced to the outer coordination sphere of the metal.⁷² This provided the first structural evidence for the type of complexes that were involved in the extraction processes. Similarly, BTP complexes of 1:3 stoichiometry were also observed with La(III), Ce(III), and U(III) iodides and triflates.⁷³ The formation of highly lipophilic 1:3 complexes with the BTPs in the presence of nitrate ions, rather than the 1:1 or 1:2 complexes observed with related tridentate *N*-donor ligands, is likely to be responsible for the greatly improved extraction by this remarkable class of ligands. Quantum mechanics calculations suggest that it is possible to tune the affinity (and basicity) of the BTP ligands through substituent effects,⁷⁴ although this remains to be studied in solvent extraction.

Numerous studies also point to the formation of 1:3 complexes by the BTPs in solution. Electrospray ionization mass spectrometry and time-resolved laser-induced luminescence studies of the complexation of BTPs with Ln(III) in acidic H_2O –MeOH solutions showed the presence of stable $Ln(BTP)_3^{3+}$ complexes. In the more-relevant diluent, octan-1-ol, complexes of 1:1, 1:2, and 1:3 stoichiometries were observed in different relative abundances depending on the lanthanide and the ligand/metal ratio used.⁷⁵ In comparison, Am(III), Cm(III), and Pu(III) exclusively formed 1:3 complexes with the BTPs which were thermodynamically more stable than the 1:3 complexes formed with Eu(III).^{76,56} The difference in stability is mainly enthalpic, pointing to a stronger bonding interaction of the BTPs with An(III) than with Ln(III).

Unusual X-ray crystallographic structures of both 1:1 and 1:2 BTP complexes with the linear uranyl cation (UO_2^{2+}) have been reported.⁷⁷ Density functional theory calculations for the 1:1 complexes showed that the bonding energy in the corresponding TERPY complex was more negative than in the BTP complex, and TERPY made a greater orbital contribution to the bonding than BTP. However, the nature of the orbitals involved differed between the two complexes. In the TERPY complex, the bonding was essentially between the UO_2^{2+} ion and the nitrate ion or between the UO_2^{2+} ion and TERPY, whereas in the BTP complex, a molecular orbital interaction involving the UO_2^{2+} ion, nitrate ions, and the triazine rings was found. In this orbital, the lone pair of the nitrogen adjacent to the ligating nitrogen of the triazine ring contributes to the bonding, suggesting that this nitrogen plays an important role in the high selectivity of the BTPs towards An(III). For a series of tridentate *N*-heterocyclic ligands, ab initio calculations of trivalent lanthanide complexes showed that complex stability increases as the electron donor ability of the central nitrogen increases and as the electron acceptor ability of the lateral nitrogens increases.⁷⁸ A thermodynamic model has been developed suggesting that for ADPTZ (**35**), the complexation with

Ln(III) is enthalpy driven, whereas for BTPs, the complexation is entropy driven.

The behavior of BTPs in their neutral, protonated, and complexed forms at oil/water interfaces has been investigated using molecular dynamics simulations. It was found that the neutral ligands were weakly surface active, whereas the protonated ligands strongly adsorbed at the interfaces with neutral or acidic water.⁷⁹ Interestingly, the NH⁺ groups of the protonated ligands point towards the oil phase, rather than the aqueous phase. It appears that complexation occurs right at the interface via the protonated

ligand, explaining why the extraction of Am(III) and Eu(III) increases as the concentration of HNO₃ increases. The 1:3 complexes Eu(BTP)₃³⁺ were also highly surface active and attracted by water at the interface. The role of synergists, such as long-chain carboxylic acids and dicarboxylate anions, appears to be to promote the formation and extraction of the 1:3 complexes adsorbed at the interface by attracting the Eu³⁺ and BTPH⁺ cations which would otherwise repel each other.⁸⁰

Table 6 2,6-Bis(1,2,4-triazin-3-yl)pyridine and Related Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides

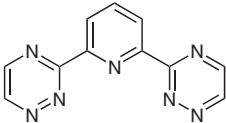
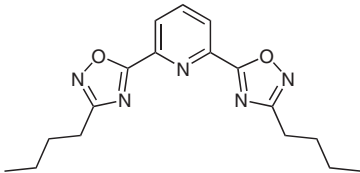
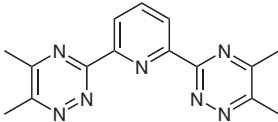
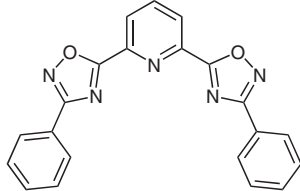
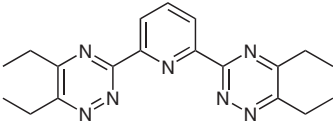
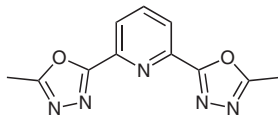
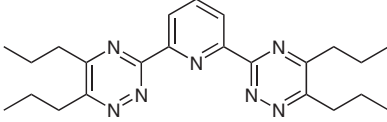
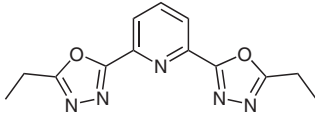
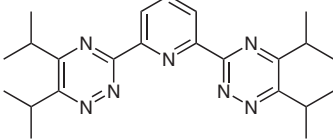
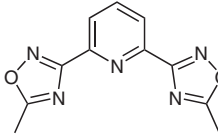
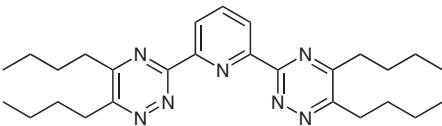
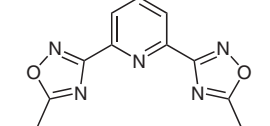
Ligand structure	Ref.	Ligand structure	Ref.
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67		84	
	65,69,73,74,75a,b,c,76b,77,78,85,91		66
68		85	
	65,69,82b,84,85,91		66
69		86	
	56,65,67,68,72,73,75,76a,c,d,77,98		66
70		87	
	67,75a,b,c,79,80		66
71		88	
	65,82a		66
72		89	

Table 6 2,6-Bis(1,2,4-triazin-3-yl)pyridine and Related Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides (continued)

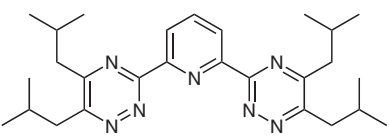
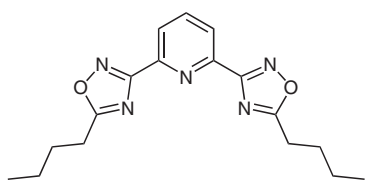
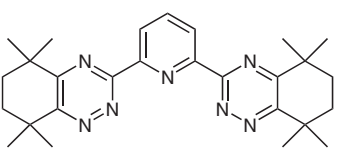
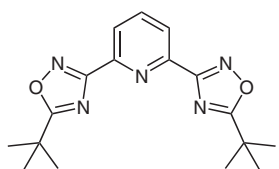
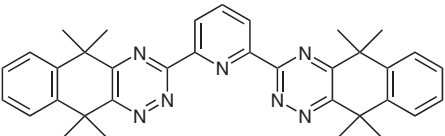
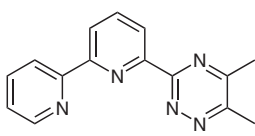
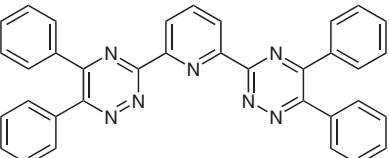
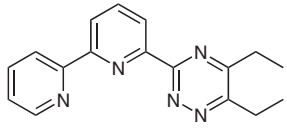
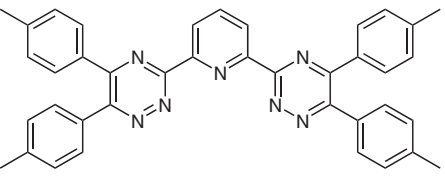
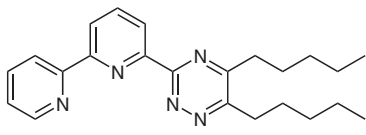
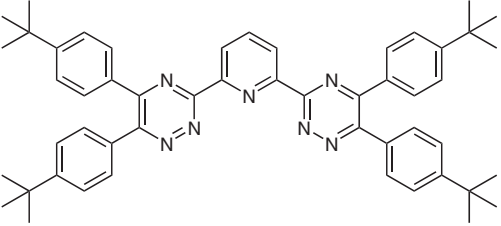
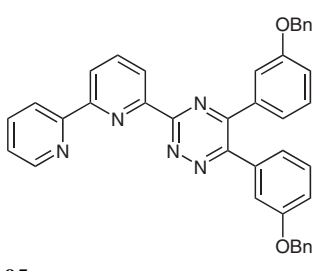
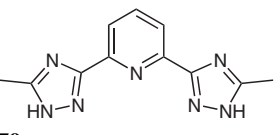
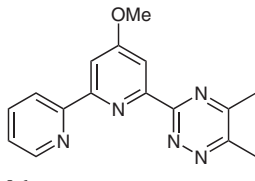
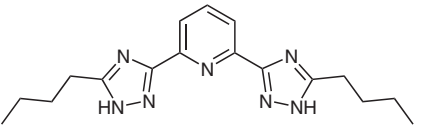
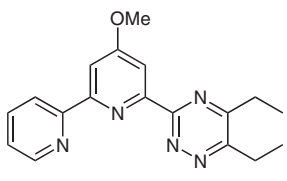
Ligand structure	Ref.	Ligand structure	Ref.
	65,69		66
73		90	
	74,79,117		66
74		91	
	117		85,88,91
75		92	
	65,85		85,88,89,91
76		93	
	65		91,98
77		94	
	65		89
78		95	
	65,71		91
79		96	
	65,71		91
80		97	

Table 6 2,6-Bis(1,2,4-triazin-3-yl)pyridine and Related Ligands Studied for Their Ability To Extract and Separate Trivalent Actinides from Lanthanides (continued)

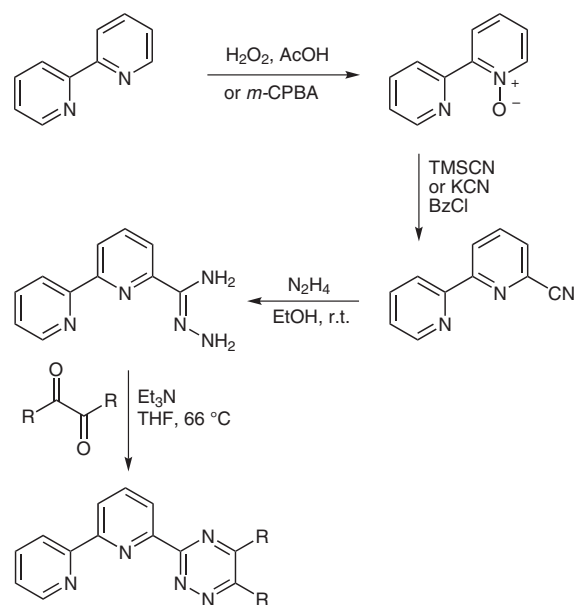
Ligand structure	Ref.	Ligand structure	Ref.
	65		92
	66		92
	66		90

Laboratory-scale SANEX processes were designed and successfully implemented using the tetrapropyl- and tetraisopropyl-substituted BTPs **70** and **71**, respectively (Table 6).⁸¹ Promising results have also been obtained in the separation of Am(III) from Ln(III) by BTPs immobilized on silica-based resins and supported liquid membranes.⁸² However, in further process development studies it was found that the tetraalkyl-substituted BTPs were susceptible to acid-catalyzed hydrolysis and radiolytic degradation leading to a decrease in the extraction performance of the diluent.⁸³ This ultimately renders these ligands unsuitable for industrial use, although it has been shown that the addition of nitrobenzene to the organic phase appears to increase the radiolytic stability of the BTPs by acting as a radical scavenger.⁸⁴

At this point, multiple parallel syntheses were carried out to form a library of 1,2,4-triazine-containing *N*-heterocycles in order to identify new ligands for the partitioning of An(III) from Ln(III).⁸⁵ The ligands were synthesized by condensing hydrazonamides with 1,2-diketones, the hydrazonamides being prepared by the reaction of hydrazine with either a pyridine-2-carbonitrile or dithiooxamide.⁸⁶ The pyridine-2-carbonitriles were in turn synthesized by the oxidation of the parent pyridines using hydrogen peroxide in acetic acid or *m*-CPBA in CH₂Cl₂, followed by a modified Reissert–Henze reaction of the resulting pyridine *N*-oxides.⁸⁷ The best results were observed for the tridentate BTPs and 6-(1,2,4-triazin-3-yl)-2,2'-bipyridines (hemi-BTPs), in which one of the triazine rings of the BTPs is replaced by a pyridine ring (Scheme 7). None of the bidentate ligands showed any useful extraction prop-

erties or Am/Eu selectivity. The hemi-BTP ligands were subsequently chosen for further study.

It was found that the hemi-BTPs have properties intermediate between those of the TERPY ligands and the BTPs and resemble more closely the former ligands.⁸⁸ Although useful selectivities were observed ($SF_{Am/Eu} \leq 30$), diethyl-substituted hemi-BTP **93** (Table 6) could only extract from HNO₃ solutions of low acidity ([HNO₃] ≤ 0.1 M) and in the presence of the synergist 2-bromodecanoic acid. Similarly, bis[(benzyloxy)phenyl]-substituted hemi-BTP

**Scheme 7** Synthesis of 6-(1,2,4-triazin-3-yl)-2,2'-bipyridine ligands

95 selectively extracted Am(III) only from weakly acidic aqueous solutions into octan-1-ol or nitrobenzene in synergistic combination with chlorinated cobalt dicarbollide, which acts as a hydrophobic anion source.⁸⁹

The formation of both 1:1 and 1:2 complexes of the hemi-BTPs with lanthanide(III) nitrates was observed by ¹H NMR spectroscopic titrations and X-ray crystallography, but, unlike the BTPs, there was no evidence for the formation of the more-hydrophobic 1:3 complexes. In addition, the ligands were susceptible to decomposition via hydrolysis of the triazine ring in a mixture of nitrous acid and nitric acid.⁸⁸

Replacing the 1,2,4-triazine ring of the hemi-BTPs with a pyrazol-1-yl ring did not improve the extraction properties, and the resulting ligand **100** (Table 6) only extracted Am(III) and Eu(III) from weakly acidic solutions with modest selectivity ($SF_{Am/Eu} \leq 8$).⁹⁰

The extraction of various transition metals and other metals [e.g., Mn(II), Ni(II), Sr(II), Zr(IV), Ru(II), Cd(II), Pb(II), and Ba(II)] by the BTP and the hemi-BTP ligands was investigated since many of these elements are present in the raffinate produced by the PUREX process. Using BTP **69** and hemi-BTP **94**, many of these metals were extracted into the organic phase with *D* values in some cases higher than those observed for Am(III).⁹¹ This is significant because these metals in high enough concentrations could disrupt an Am(III) extraction process by sequestering the extractant. A number of homoleptic octahedral complexes of the hemi-BTPs with manganese(II), iron(II), cobalt(II), and zinc(II) were also characterized by X-ray crystallography.

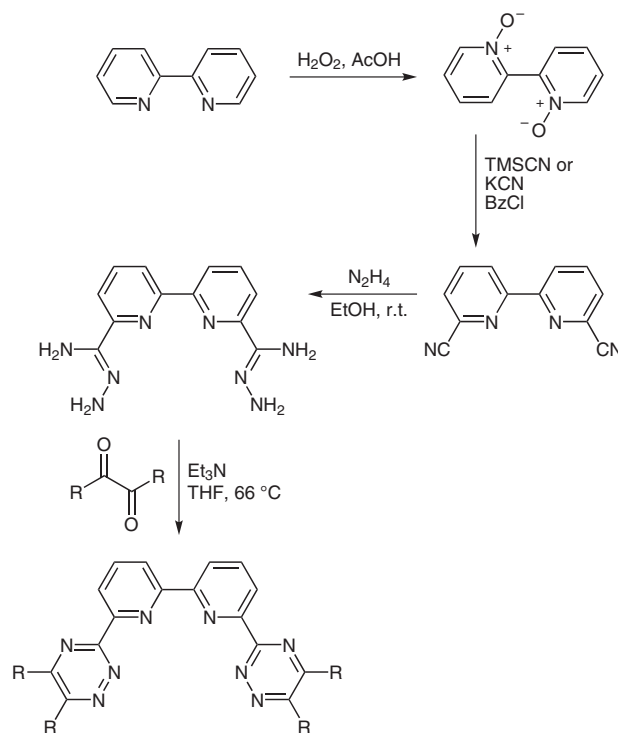
Tridentate ligands possessing two outer 1,3,5-triazine rings were then studied to determine if the presence of the two adjacent nitrogen atoms in the 1,2,4-triazine rings of the BTPs was responsible for the superior properties of the BTP ligands. 2,6-Bis(1,3,5-triazin-2-yl)pyridines **98** and **99** (Table 6) were synthesized by the reaction of pyridine-2,6-dicarbonitrile and dicyandiamide (cyanoguanidine), followed by acylation of the amino groups with pivaloyl chloride in the case of **99**. In solvent extraction experiments, the performance of **98** and **99** was considerably worse than that of the BTPs under similar conditions either in the presence or absence of a synergist.⁹² Very low distribution ratios and only moderate separation factors ($SF_{Am/Eu} \leq 6$) were observed. This study suggested that the unique properties of the BTPs are indeed related to the presence of the two adjacent nitrogen atoms in the triazine rings.

8 6,6'-Bis(1,2,4-triazin-3-yl)-2,2'-bipyridine (BTBP) and Related Ligands

The susceptibility of the BTP ligands to hydrolysis and radiolysis prompted us to investigate analogous tetradentate (or quadridentate) ligands. The process development studies on the BTPs also revealed that the back-extraction

(stripping) of An(III) from a loaded organic phase could not be accomplished. This was probably due to the ability of three BTP ligands to enclose completely the inner coordination sphere of the metal. However, a tetradentate bis-triazine ligand would be expected to have a weaker ligand field and perhaps form less-stable 1:1 and/or 1:2 complexes, leaving sufficient room for water, nitrate, or stripping agents to coordinate to the metal and displace the ligands. 6,6'-Bis(1,2,4-triazin-3-yl)-2,2'-bipyridine (BTBP) ligands were subsequently investigated.

The BTBP ligands are typically synthesized as shown in Scheme 8. Oxidation of 2,2'-bipyridine with hydrogen peroxide in acetic acid⁹³ and the Reissert–Henze reaction of the resulting bis-*N*-oxide affords the corresponding dinitrile.⁹⁴ The addition of hydrazine to the dinitrile generates the dicarbohydrazonamide,⁶⁴ which is condensed with a 1,2-diketone to form the BTBP. Some BTBP ligands have previously been employed as synthetic precursors to substituted quaterpyridine ligands.⁶⁴



Scheme 8 Synthesis of 6,6'-bis(1,2,4-triazin-3-yl)-2,2'-bipyridine ligands

The BTBP and related ligands that were synthesized and tested for their ability to selectively extract Am(III) from Eu(III) are shown in Table 7.

Initial studies with tetraethyl-substituted BTBP **102** showed promising results. Both high affinity for Am(III) ($D_{Am} = 650 \pm 33$) and high selectivity for Am(III) over Eu(III) ($SF_{Am/Eu} = 160 \pm 16$) were observed in the extraction of the metals from 1 M HNO₃ using a 0.068 M solution of **102** in 1,1,2,2-tetrachloroethane.⁹⁵ The somewhat slow kinetics of the extraction could be accelerated using phase-transfer reagents.⁹⁶

Lanthanide nitrate complexes of the formula $[\text{Ln}(\text{L})(\text{NO}_3)_3]$ were synthesized and characterized by X-ray crystallography. The structures showed the lanthanides were coordinated to one planar tetradentate BTBP ligand and three bidentate nitrate ions in a 10-coordinate environment of C_2 symmetry.⁹⁷ No solid state evidence was observed for the formation of 1:2 complexes, but NMR spectroscopic titrations with $\text{La}(\text{NO}_3)_3$ and yttrium nitrate $[\text{Y}(\text{NO}_3)_3]$ showed the presence of both 1:1 and 1:2 complexes in solution. Further evidence for the formation of complexes of these stoichiometries was obtained from spectrophotometric titrations of tetrapentyl-substituted BTBP **105** and bis(tetramethylcyclohexane)-fused BTBP $\text{CyMe}_4\text{-BTBP}$ (**107**) with $\text{La}(\text{III})$, $\text{Eu}(\text{III})$, and $\text{Yb}(\text{III})$ in methanol.⁹⁸ However, only the 1:2 complexes of $\text{CyMe}_4\text{-BTBP}$ (**107**) and tetrapentyl-substituted BTBP **105** with $\text{Am}(\text{III})$ in various diluents were observed by electrospray ionization mass spectrometry.⁹⁹

Table 7 6,6'-Bis(1,2,4-triazin-3-yl)-2,2'-bipyridine and Related Ligands Studied for Their Ability to Extract and Separate Trivalent Actinides from Lanthanides

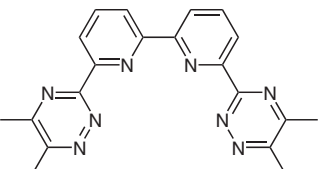
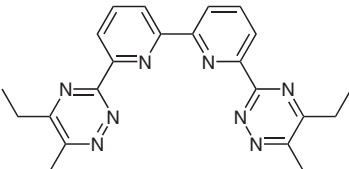
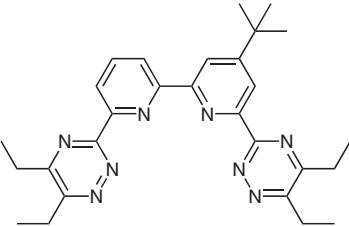
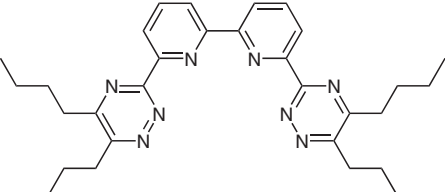
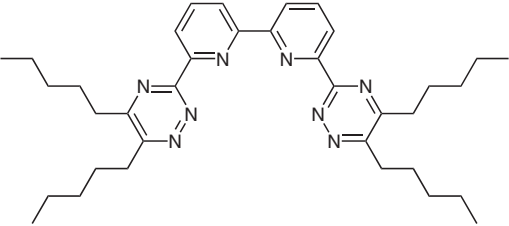
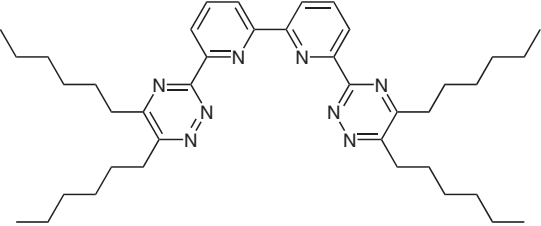
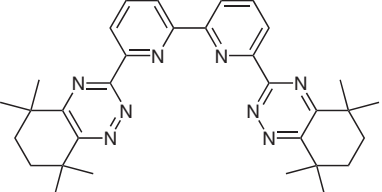
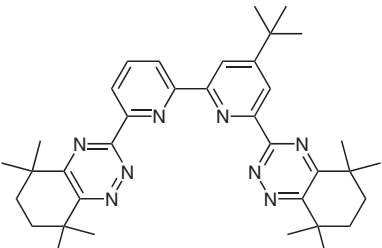
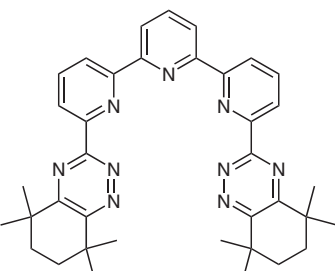
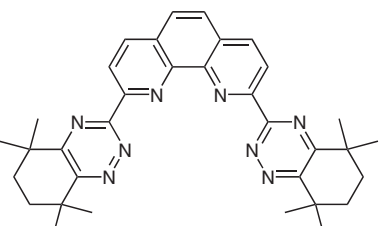
Ligand structure	Ref.
	109b,117
101	
	95–97,102, 103,111,118
102	
	110,111,118
103	
	97,102
104	

Table 7 6,6'-Bis(1,2,4-triazin-3-yl)-2,2'-bipyridine and Related Ligands Studied for Their Ability to Extract and Separate Trivalent Actinides from Lanthanides (continued)

Ligand structure	Ref.
	97–103,107, 116,118,119
105	
	97,102
106	
	77,97–99, 102,104–109,111,118, 119,121
107	
	111,118,120
108	
	112
109	
	113
110	

Further detailed solvent extraction studies were carried out on more-lipophilic BTBPs bearing longer alkyl side chains. Tetrapentyl-substituted BTBP **105** showed variable distribution ratios, but high separation factors in the extraction of Am(III) and Eu(III) into a range of organic diluents which suggested that back-extraction of the metals would be possible through careful choice of diluent and by adjusting the acidity of the aqueous phase.¹⁰⁰ The most suitable diluent was cyclohexanone and rapid extraction kinetics were observed in this diluent (equilibrium was reached within 5 min).¹⁰¹ Another feature of the BTBPs is that, like the BTPs, the extraction of both Am(III) and Eu(III) increases as the concentration of HNO₃ increases.

The thermodynamics of the extraction showed that Am(III) had a more negative Gibbs free energy of extraction than Eu(III). Back-extraction of Am(III) using glycolic acid and recycling of the organic phase were successfully demonstrated showing that, unlike the BTP ligands, a continuous extraction process was feasible. However, ligand **105** was sensitive to radiolysis and D_{Am} decreased by about 80% on exposure of the diluent to approximately 17 kGy of gamma radiation.¹⁰⁰

The extraction of Am(III), Th(IV), Np(V), and U(VI) by a range of BTBP ligands has been investigated to determine the effect of the oxidation state of the actinide ions on their extraction.¹⁰² It was found that the extraction increased in the order Am(III) < Th(IV) < Np(V) < U(VI) at low BTBP concentrations, but increased in the order Th(IV) < U(VI) < Np(V) < Am(III) at high BTBP concentrations. This study suggests that the tri- and pentavalent actinides can be separated from the tetra- and hexavalent actinides using the BTBPs. In addition, the BTBPs also extracted several d-block metals to a significant extent, in common with the tridentate BTP and hemi-BTP ligands.^{100,103}

The most promising of the BTBP ligands is CyMe₄-BTBP (**107**), which was designed to be more resistant to radiolysis (discussed in detail in Section 9). This ligand is the most studied of the BTBP ligands, and its solvent extraction chemistry has been looked at in detail.¹⁰⁴ Using this ligand, high selectivities were observed for Am(III) and Cm(III) over the entire lanthanide series as well as yttrium. When dissolved in octan-1-ol (0.02 M), the ligand gave a D_{Am} value of approximately 4.5 and an $\text{SF}_{\text{Am/Eu}}$ of about 140 in the extraction of Am(III) and Eu(III) from 0.5 M HNO₃, and equilibrium was reached within 60 minutes. The slow kinetics of the extraction were considerably improved by the addition of DMDOHEMA (**4**) (see Figure 1) to the organic phase, and equilibrium was reached after only 5 minutes. The dependence of D_{Am} on the concentration of CyMe₄-BTBP (**107**) showed the metals were extracted as 1:2 complexes. The ligand showed excellent hydrolytic stability on long-term (2 months) exposure to 1 M HNO₃ with no reduction in the D values or $\text{SF}_{\text{Am/Eu}}$. In addition, the selective back-extraction of the lanthanides (scrubbing) followed by the actinides (strip-

ping) was accomplished using aqueous solutions of 0.5 M HNO₃ and 0.5 M glycolic acid at pH 4, respectively.

After some optimization of the conditions,¹⁰⁵ a laboratory-scale SANEX process was successfully demonstrated on a genuine spent fuel solution using CyMe₄-BTBP (**107**) and DMDOHEMA (**4**) dissolved in octan-1-ol.¹⁰⁶ The countercurrent extraction process was carried out in centrifugal contactors and comprised 16 stages (9 stages for extraction, 3 stages for lanthanide back-extraction, and 4 stages for actinide back-extraction). More than 99.9% of Am(III) and Cm(III) were recovered from the 2 M HNO₃ feed solution and more than 99.9% of the lanthanides were directed to the raffinate.

The ligand CyMe₄-BTBP (**107**) has also been investigated as a potential ligand for a GANEX (Group Actinide EXtraction) separation process. The intention of this process is to extract the actinides directly from the PUREX raffinate, removing the need for a preceding DIAMEX process. Under these conditions, the actinides need to be extracted in different oxidation states and the metal loading of the aqueous phase will be far higher than in a SANEX process. Under process-like conditions, solutions of CyMe₄-BTBP (**107**) and tributyl phosphate (**1**) (used in the PUREX process) in cyclohexanone selectively extracted Am, Pu, Np, and U from 4 M HNO₃ solutions of high metal loading (>9000 ppm),¹⁰⁷ suggesting that such a GANEX process is feasible. It was shown that each ligand extracted independently of the other and no synergistic effects were observed.

The first crystal structures of actinide complexes of CyMe₄-BTBP (**107**) have been reported. Treatment of the ligand with the uranyl salts UO₂(OTf)₂ and UO₂I₂(THF)₃ under anhydrous conditions led to the formation of mononuclear 1:1 complexes in which the ligand coordinates to the metal in a tetradentate fashion perpendicular to the plane of the UO₂²⁺ ion.¹⁰⁸ In the presence of moist air, the complexes crystallized as dinuclear structures [(UO₂L)–O–(UO₂L)²⁺] containing a flexible μ -oxo bridge. Mononuclear 1:1 complexes of **107** were also obtained with tetravalent Cp*₂U²⁺ ions (Cp* = pentamethylcyclopentadienyl) and with pentavalent UO₂⁺ ions that were formed by the reduction of the corresponding UO₂²⁺ complexes with (pentamethylcyclopentadienyl)potassium or cyclopentadienylthallium.¹⁰⁹ A very unusual dinuclear μ -oxo mixed-valence U(IV)/U(VI) complex was isolated from a mixture of U(OTf)₄, UO₂(NO₃)₂, and CyMe₄-BTBP (**107**).⁷⁷ In this complex, two ligands of **107** coordinated to the U(IV) ion in an orthogonal arrangement, while the nitrates coordinated to the U(VI) ion.

A comparative investigation of the complexation of Cm(III) and Eu(III) by *tert*-butyl-substituted BTBP **103** using TRLFS was carried out under conditions relevant to the extraction process. Complexes of 1:2 stoichiometry were observed for both metal ions, but the stability constant for the Cm(III) complex was found to be approximately two orders of magnitude higher than that for the Eu(III) complex.¹¹⁰ The enthalpy of complexation of

Cm(III) was more negative than that of Eu(III), while the entropy of complexation of both metal ions was very similar. This study showed that the remarkably high selectivity of the BTBPs towards An(III) over Ln(III) was driven by the greater thermodynamic stability of their complexes with An(III).

Recent quantum mechanics calculations showed that the BTBPs are less basic and afford complexes that are less thermodynamically stable than those of their rigidified phenanthroline (BTPhen) analogues. Molecular dynamics simulations at the oil/water interface revealed that CyMe₄-BTBP (**107**) is only surface active when protonated and when complexed to a single Eu(III) cation.¹¹¹ As with the BTPs, the NH⁺ group of the protonated BTBP ligand **107** orients away from the aqueous phase to avoid hydrophobic contact with the aliphatic rings. These results suggest that the extraction of Am(III) and Eu(III) by **107** takes place at the interface via the protonated ligand under acidic conditions and explain why the extraction kinetics are slow in the absence of a phase-transfer agent.

In an effort to understand better the origins of the high selectivity of bis-triazine ligands towards An over Ln, pentadentate ligand **109**, which contains an additional pyridine ring compared with CyMe₄-BTBP (**107**), was investigated. Although mildly selective ($SF_{Am/Eu} \leq 12$), the ligand was essentially unable to extract Am(III) or Eu(III) from HNO₃ into octan-1-ol in the absence of a synergist ($D_{Am} < 0.04$), making it less efficient than the tetradentate ligand CyMe₄-BTBP (**107**) by about two orders of magnitude.¹¹² In a nitrate medium, only the 1:1 complexes with Ln(III) were observed by NMR spectroscopy and mass spectrometry, whereas the more-hydrophobic 1:2 complexes were formed in a perchlorate medium. This indicated that nitrate ions competed with ligand **109** for coordination sites on the metal, resulting in the less-hydrophobic 1:1 complexes that were not easily extracted.

Very recently, it has been shown that the extraction performance of the tetradentate BTBP ligands can be improved considerably by pre-organizing the ligand for metal ligation using a *cis*-locked 1,10-phenanthroline moiety. Phenanthroline-derived ligand CyMe₄-BTPhen (**110**), synthesized according to the procedure shown in Scheme 9, separated Am(III) and Cm(III) from the lanthanides with very high extraction efficiency and selectivity ($D_{Am} \geq 1000$, $SF_{Am/Eu} = \text{ca. } 200\text{--}400$ from 1–4 M HNO₃) and with faster extraction kinetics (equilibrium reached within 15 min) compared with its 2,2'-bipyridine-derived counterpart **107**.¹¹³

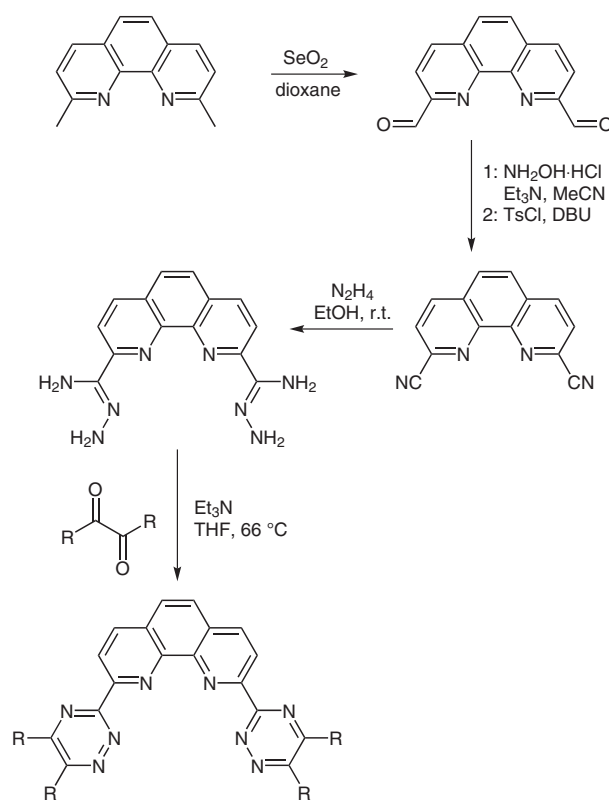
Surface tension measurements revealed that BTPhen ligand **110** was in higher concentrations at the phase interface than **107**, which explained the faster rates of extraction by **110**. In addition, **110** on treatment with Eu(NO₃)₃ formed a complex of the formula [EuL₂NO₃]²⁺[Eu(NO₃)₅]²⁻, which was the first lanthanide 1:2 bis-complex of a tetradentate bis-triazine ligand to be characterized by X-ray crystallography.

9 Improving Radiolytic Stability through Ligand Design

In a potential SANEX process, the organic and aqueous phases will be exposed to high levels of ionizing radiation owing to the presence of radioactive alpha- and gamma-emitting radionuclides. This will impact the performance of any solvent extraction processes used for nuclear fuel reprocessing, and a knowledge of such effects is critical for the design of robust solvent systems. The effects of radiation chemistry on solvent extraction processes have been reviewed.¹¹⁴ It has been estimated that the organic phase in a SANEX process will receive a total annual dose of between 100 kGy and 1 MGy, depending on the type of waste being reprocessed.⁸⁴ Direct absorption of this energy by the diluent molecules of the organic and aqueous phases leads to the formation of electronically excited states, free-radical species, solvated electrons, and ions which can subsequently react with the extractant molecules.

The radiolysis of water results in the formation of hydroxy radicals, hydrogen atoms, solvated electrons, protons, hydrogen peroxide, and hydrogen,¹¹⁵ while the radiolysis of a typical alkane-like organic diluent produces alkyl radical cations, alkyl radicals, solvated electrons, hydrogen atoms, and hydrogen.¹¹⁶

Process development studies on the tetraalkyl-substituted BTPs, such as tetraisopropyl-substituted BTP **71**, showed that the ligands were susceptible to indirect radiolysis



Scheme 9 Synthesis of 2,9-bis(1,2,4-triazin-3-yl)-1,10-phenanthroline ligands

caused by chemical attack at their reactive benzylic positions by free-radical species, resulting in side-chain degradation with detrimental effects on extraction ability and selectivity.^{83b} Furthermore, the extraction performance of tetrapentyl-substituted BTBP **105** decreased with increasing doses of gamma radiation, and the degradation products were identified by mass spectrometry.¹¹⁷ Many of the degradation products arose from hydrogen atom abstraction and subsequent oxidation of the benzylic positions, eventually leading to cleavage of the alkyl groups. The replacement of the labile benzylic hydrogens with alkyl groups thus became the primary goal in the design and synthesis of selective actinide extractants with improved resistance to radiolysis.

Subsequently, attempts were made to synthesize a BTP ligand containing *tert*-butyl groups attached to the triazine rings rather than primary alkyl groups. Unfortunately, the condensation reaction of pivalil (2,2,5,5-tetramethylhexane-3,4-dione) with pyridine-2,6-dicarbohydrazonamide (Scheme 6, R = *t*-Bu) failed to afford the desired ligand, probably owing to the sterically hindered nature of the 1,2-diketone or its inability to adopt the *cis*-conformation required for the condensation reaction.

It was reasoned that a cyclic 1,2-diketone would be more reactive as the carbonyl groups would be locked in the required *cis*-conformation. Gratifyingly, the reaction of pyridine-2,6-dicarbohydrazonamide with the cyclic 1,2-diketones 3,3,6,6-tetramethylcyclohexane-1,2-dione and 1,1,4,4-tetramethylnaphthalene-2,3-dione gave the related annulated BTP ligands CyMe₄-BTP (**74**) and BzCyMe₄-BTP (**75**), respectively (see Table 6), in high yields.¹¹⁸

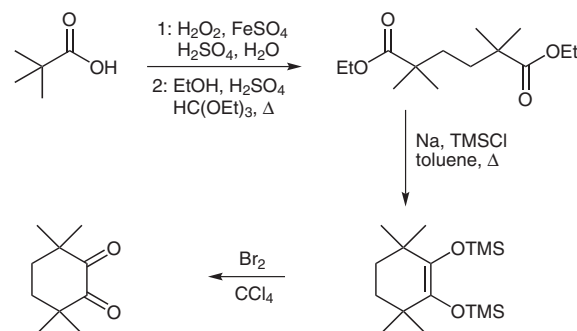
In solvent extraction experiments, CyMe₄-BTP (**74**) proved to be a more effective extractant than tetraisopropyl-substituted BTP **71** in the presence of the phase modifier DMDOHEMA (**4**). Typically, for 0.01 M solutions of the ligands in octan-1-ol after 15 minutes of phase contact with 0.5 M HNO₃, values for D_{Am} of approximately 500 and $SF_{\text{Am/Eu}}$ of about 5000 using CyMe₄-BTP (**74**) were achieved, whereas D_{Am} was about 30 and $SF_{\text{Am/Eu}}$ approximately 400 using tetraisopropyl-substituted BTP **71**. For BzCyMe₄-BTP (**75**), values for D_{Am} of approximately 10 and $SF_{\text{Am/Eu}}$ of about 500 were obtained under identical conditions.¹¹⁸ The remarkably high selectivity for Am(III) over Eu(III) of CyMe₄-BTP (**74**) was far in excess of what was observed with other *N*-donor ligands. The formation of the expected 1:3 complexes of **74** with the lanthanides was confirmed by ¹H NMR spectroscopic titrations and X-ray crystallography.

In contrast to other BTPs, both annulated BTPs **74** and **75** were stable to hydrolysis and were not hydrolyzed by boiling HNO₃ (3 M) over 24 hours. After exposure of octan-1-ol solutions of the ligands to 100 kGy of gamma radiation, there was significant degradation of CyMe₄-BTP (**74**) and tetraisopropyl-substituted BTP **71** (ca. 80%), but no degradation of BzCyMe₄-BTP (**75**) occurred. It is thought that the additional aromatic rings present in **75**

compared with **74** are able to dissipate some of the energy absorbed by the ligand during direct radiolysis. Theoretical simulations of electron loss and gain on various fragments of **74** and **75** suggest that upon electron loss (as would occur during direct radiolysis), most of the charge resides in the benzene rings of **75** (64%), but in the triazine rings of **74** (45%). This view is supported by frontier orbital calculations, which show that there are two pairs of doubly degenerate highest occupied molecular orbitals localized on the outer benzene rings of **75** which are not present in **74**.¹¹⁸

The stability of the tetradentate ligand CyMe₄-BTBP (**107**) and its more-soluble¹¹⁹ 4-*tert*-butyl-substituted derivative MF2-BTBP (**108**) (Table 7) towards radiolysis was then investigated. When exposed to low doses of gamma irradiation (<30 kGy), CyMe₄-BTBP (**107**) dissolved in hexanol or cyclohexanone showed good stability and the extraction of Am(III) and Eu(III) remained largely unaffected. In contrast, the extraction efficiency of tetrapentyl-substituted BTBP **105**, which has benzylic hydrogens, decreased as the total absorbed dose increased under the same conditions.¹²⁰ However, the resistance of MF2-BTBP (**108**) dissolved in cyclohexanone towards gamma radiolysis was found to depend on the dose rate. At low dose rates (ca. 15 Gy/h), the extraction of Am(III) and Eu(III) by MF2-BTBP (**108**) was more or less unchanged up to an absorbed dose of 100 kGy, but at high dose rates (ca. 1.2 kGy/h), the extraction of Am(III) and Eu(III) decreased with increasing dose, indicating that secondary processes (indirect radiolysis) were likely to be responsible for the degradation rather than the radiation directly.¹²¹ In a similar study, CyMe₄-BTBP (**107**) in octan-1-ol was more sensitive to gamma radiolysis (0.22 kGy/h) than to alpha radiolysis (1 kGy/h), and the rate of degradation of **107** was 40% higher when exposed to gamma radiation.¹²²

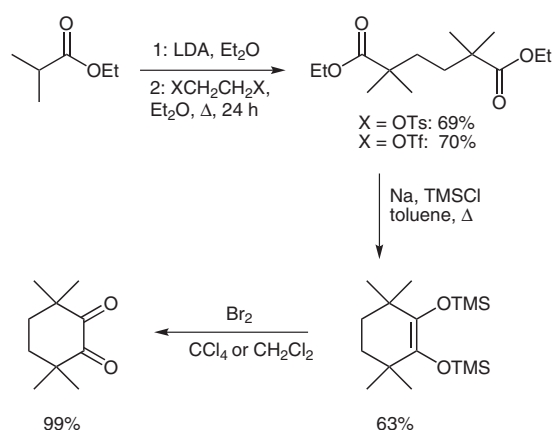
During initial studies, a serious drawback of working with CyMe₄-BTP (**74**), CyMe₄-BTBP (**107**), MF2-BTBP (**108**), and CyMe₄-BTPhen (**110**) was the difficulty encountered in synthesizing large quantities of the ligands for process development studies. This was due to the relatively inefficient method of synthesizing the 1,2-diketone precursor (Scheme 10). The first step of this synthesis involves the generation of 2,2,5,5-tetramethyl adipic acid by the free-radical dimerization of pivalic acid



Scheme 10 Synthesis of 3,3,6,6-tetramethylcyclohexane-1,2-dione

mediated by Fenton's reagent (H_2O_2 and FeSO_4).¹²³ This reaction is reported to give yields of approximately 37%, but in our hands, yields of 15% or lower were obtained, particularly when attempting scale-up. The diacid is then esterified and the diester is cyclized by an intramolecular acyloin reaction using sodium and chlorotrimethylsilane in toluene. Oxidation of the resulting bis(silyl ether) of the enediolate with bromine then affords 3,3,6,6-tetramethylcyclohexane-1,2-dione. The acyloin reaction may also be carried out in the absence of chlorotrimethylsilane to generate the α -hydroxy ketone, which is then oxidized to the 1,2-diketone using copper(II) acetate.¹²⁴

Although suitable for synthesizing small quantities of **74**, **107**, **108**, and **110**, the above synthetic route proved impractical for large-scale synthesis and thus presented a barrier to the application of the ligands in an industrial SANEX process. Subsequently, a more efficient and scaleable synthesis of 3,3,6,6-tetramethylcyclohexane-1,2-dione was developed (Scheme 11) which bypasses the problematic first step in the previous method.^{113,125} Using this new method, alkylation of the enolate of ethyl isobutyrate with disulfonate esters derived from ethylene glycol afforded the diester intermediate in good yields (69–70%).



Scheme 11 Modified and improved synthesis of 3,3,6,6-tetramethylcyclohexane-1,2-dione

When the alkylation reaction was conducted using 1,2-dihalides as electrophiles, mixtures of products were obtained of which the major product was the corresponding ethyl α -haloisobutyrate, formed by the attack of the hindered enolate on a halogen atom with subsequent elimination of ethene.¹²⁶ Completion of the synthesis as before (intramolecular acyloin reaction/oxidation) yielded the 1,2-diketone in significantly higher yields than those obtained using the previous method (44% overall compared to <5% overall). This facile synthesis of the diketone precursor to CyMe_4 -based ligands, such as **74**, **107**, **108**, and **110**, removed one of the biggest obstacles to the development of an industrial SANEX process, namely, the ability to synthesize the ligands on a large scale.

10 Conclusion and Outlook

In summary, we have surveyed recent advances in Europe in the design, synthesis, study, and development of soft *N*- and *S*-donor ligands for separating actinides from lanthanides in the nuclear fuel cycle. Bis-1,2,4-triazine-containing compounds composed only of the elements carbon, hydrogen, oxygen, and nitrogen have emerged as the most promising family of ligands for this purpose, showing levels of selectivity between the chemically similar actinides and lanthanides once thought impossible to achieve.

These reagents and their extracted metal complexes possess a high enough range of solubilities in suitable diluents, such as octan-1-ol, for use in the SANEX process. Optimum levels of affinity that permit the back-extraction of the metals have been achieved with the BTBP ligands. The BTBPs are not susceptible to hydrolysis and are resistant to radiolysis at low dose rates. The ease of synthesis of these reagents has been recently improved, and CyMe_4 -BTBP (**107**) and related ligands are now commercially available in quantities ranging from kilograms to tonnes.¹²⁷ Furthermore, the ligands are capable of extracting from solutions of high acidity.

The considerable advances of recent years, both in process demonstrations as well as in molecular-level understanding, set the stage for the development of even more efficient and robust ligands for use in more-demanding future actinide/lanthanide separation processes (e.g., the GANEX process).

Acknowledgment

We are grateful to the Nuclear Fission Safety Program of the European Union for support under the ACSEPT (FP7-CP-2007-211 267) contract.

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