Computational-Aided Design of Next-Generation Extractants for Trivalent Actinide and Lanthanide Separation

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Article

Keywords:

Posted Date: May 7th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-4355272/v1
Computational-Aided Design of Next-Generation Extractants for Trivalent Actinide and Lanthanide Separation

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Abstract

The chemical similarities between trivalent actinides (An(III)) and lanthanides (Ln(III)) stemming from their analogous ionic radii and physicochemical properties present a significant challenge in differentiating and separating them via solvent extraction, which is a pressing issue in nuclear and radiochemistry. However, the existing approaches suffer from different drawbacks such as inadequate separation factors, limited stripping efficiency, and undesired co-extraction. In this study, a novel unsymmetrical phenanthroline-derived amide-triazine (Et-Tol-CyMe_4-ATPhen) extractant was designed with the aid of theoretical calculations and synthesized using an unprecedented de novo construction method. As expected, the Et-Tol-CyMe_4-ATPhen extractant exhibited a favorable extraction ability for Am(III) and minimal extraction for Ln(III), thereby achieving an extremely selective An(III)/Ln(III) separation with a separation factor over 280. Furthermore, Am(III) could be effectively stripped from loaded phases using dilute nitric acid. The underlying coordination mechanisms were thoroughly elucidated by using ^1H NMR, ESI-MS, UV-Vis absorption spectrum, fluorescence excitation spectrum, and X-ray single-crystal diffraction. This work holds promise for addressing the current challenges in An(III)/Ln(III) separation and represents a pioneering endeavor in developing next-generation extractants from first principles calculation.

Graphic Abstract
Introduction

Lanthanides and actinides, defined by 4f and 5f electrons, compose the f-block elements. The lanthanide series spans La to Lu, primarily as stable Ln(III) ions in water. Th, U, Np, and Pu commonly show oxidation states of +4, +6, +5, and +4 in aqueous phase. Other actinides mainly exist as stable An(III) ions in acidic conditions. Americium and subsequent minor actinides like Cm and Cf are produced in nuclear reactors from neutron capture of uranium. Extracting minor actinides from SNF for recycling or transmutation aligns with environmental protection and nuclear safety imperatives. Lanthanides, as high neutron-capture fission products (e.g., $^{149}$Sm, $^{157}$Gd) in SNF, and their coexistence hinder efficient transmutation and utilization of minor actinides, emphasizing the need for effective separation between them.

However, the efficient separation of An(III)/Ln(III) via solvent extraction remains a challenging issue. This challenge stems from the closely similar outer electronic configurations, same valence states, and comparable ionic radii of these elements, resulting in nearly identical chemical behaviors. According to the hard-soft acid-base (HSAB) theory, An(III) species with more diffuse 5f electron orbitals exhibit softer acid character compared to their 4f Ln(III) counterparts. Therefore, An(III) ions show a stronger affinity towards soft donor bases like N or S, supporting the rationale for employing lipophilic extractants with N or S donor atoms for An(III)/Ln(III) separation.

Before 1999, there were no extractants capable of separating trivalent actinides and lanthanides under high acid conditions until 2,6-bis(1,2,4-triazin-3-yl)pyridine (BTP) ligands was discovered. However, BTP’s stability under strong acidity and irradiation remains unsatisfactory. A promising tetradeinate 6,6'-bis(1,2,4-triazin-3-yl)-2,2'-bipyridine ligands (BTBP) derivatives were found to show robust Am(III)/Eu(III) separation in low-polarity solvents. Yet, the slow extraction kinetics resulted from the rotatable bipyridine skeleton necessitated the addition of malonamide ligands to facilitate the metals transferring from aqueous solution to organic phase. Modification led to a rigid 2,9-bis(1,2,4-triazin-3-yl)-1,10-phenanthroline (BTPhen) extractant with expedited kinetics and improved extraction capability, but the co-extraction with Ln(III) and high Am(III) distribution ratios pose
stripping challenges\textsuperscript{21}. Coordination chemistry experiments in solution and solid system confirmed that 1,10-phenanthroline-2,9-dicarboxamide (PDAM) held a strong affinity for Ln(III) ions with large radius with potential An(III)/Ln(III) separation ability\textsuperscript{22,23}. Therefore, the N,O-hybrid extractant N,N'-diethyl-N,N'-ditolyl-2,9-diamide-1,10-phenanthroline (Et-Tol-DAPhen) was developed by combining soft N donor atoms on phenanthroline skeleton and hard O donor atoms on amide side chains, showing a notable An(III/IV/VI)/Eu(III) separation efficacy\textsuperscript{24-26}. However, cascade countercurrent extraction revealed a periodic trend in Et-Tol-DAPhen's extraction efficiency for Ln(III) with a significant co-extraction phenomenon observed for light lanthanides\textsuperscript{27}. Meanwhile, a class of bis-lactam-1,10-phenanthroline (BLPhen) extractants developed through pre-organization modification, exhibited an enhanced Am(III) extraction capability\textsuperscript{28}. However, under high acidity conditions, noticeable co-extraction phenomena were observed for the Ln(III) ions as well\textsuperscript{29}.

At present, no such reported extractant could simultaneously combine the advantages of strong extraction ability in high acidity, complete separation ability for Am(III)/Ln(III) and convenient stripping\textsuperscript{30,31}. Meanwhile, the conventional synthesis methods for phenanthroline-derived extractants were grafting side functional groups onto phenanthroline skeleton, resulting in difficult modifications and limited novel structures\textsuperscript{32,33}. In addition, numerous studies have shown that for the extractants of An(III)/Ln(III) separation, the density functional theory (DFT) calculations accurately reproduced the separation trend observed in experiments and provided a deeper understanding of the extraction and separation mechanisms\textsuperscript{34-38}. Moreover, compared to experimental methodologies, DFT calculations require less manpower, budget, and time, allowing for rapid adjustments in extractants structures and performing corresponding calculations, thus enabling more efficient researches\textsuperscript{39,40}. Therefore, this study initially employed DFT calculations to assess the extraction and separation capabilities of proposed extractants for Am(III) and Eu(III), aiming to identify the most promising candidates.

Here, we designed three unsymmetrical extractants (2-N-ethyl-N-(tolyl)carboxamide-6-(5,5,8,8-tetramethylcyclohexyl-[1,2,4]triazin-3-yl)-pyridine (Et-Tol-CyMe\textsubscript{4}-ATP, L1), 6-N-ethyl-N-(tolyl)carboxamide-6’-(5,5,8,8-tetramethylcyclohexyl-[1,2,4]triazin-3-yl)-2,2’-
bipyridine (Et-Tol-CyMe₄-ATBP, L₂), and 2-N-ethyl-N-(tolyl)carboxamide-9-(5,5,8,8-
tetramethylcyclohexyl-[1,2,4]triazin-3-yl)-1,10-phenanthroline (Et-Tol-CyMe₄-ATPhen, L₃))
by incorporating both amide and triazine functional groups onto the N-heterocyclic skeletons,
and predicted their Am(III)/Eu(III) separation potential assisted by DFT calculation, leading to
the conclusion that L₃ is the optimal extractant. A brand-new de novo construction method was
developed to successfully synthesize this phenanthroline-derived L₃ extractant. Subsequent
solvent extraction results confirmed the DFT predictions, highlighting L₃’s most favorable
extraction for Am(III) and its convenient stripping. Furthermore, L₃ showed a weak extraction
towards all the Ln(III) ions, achieving a notable An(III)/Ln(III) separation. The coordination
mechanisms of L₃ with f-block elements were fully disclosed via various spectroscopic
methods and structural characterizations. This study provides an innovative unsymmetrical
phenanthroline-derived extractant that promises to solve the current challenges in
An(III)/Ln(III) separation.

Results and Discussion

Theoretical Design and Screening

To design the extractants that combine all the merits of extraction, stripping and selectivity
properties for An(III)/Ln(III) separation remains a big challenge. We suppose that the
unsymmetrical extractants composed of both amide and triazine functional groups onto N-
heterocyclic skeletons (pyridine, bipyridine, phenanthroline) could achieve this target.

To predict the extraction and separation capabilities of the assumed ligands for Am(III) and
Eu(III), DFT calculations were first performed on the ML-type complexes, i.e., ML(NO₃)₃ (M
= Am(III), Eu(III); L = L₁, L₂, L₃). Considering the rotation of the C-N single bond in the
amide side chain of the ligand, our calculations accounted for two isomers, labeled as is₁ and
is₂ (Fig. S2). According to their relative energies after optimization in Fig. S3, S4 and Tables
S1, S2, respectively, is₁ was identified as the most stable one for ML(NO₃)₃ complex and was
employed for subsequent calculations and discussion. For all ML(NO₃)₃-is₁ complexes, the
ligand provided three (L₁) or four (L₂, L₃) coordinating atoms, along with three nitrate ions
coordinating in a bidentate manner, resulting in a coordination number of 9 (L1) or 10 (L2, L3) for the metal center, respectively (Fig. 1a-c).

**Fig. 1.** The Am(III)/Eu(III) separation extractants designed and screened by DFT calculation.

Optimized structure of a Am(L1)(NO$_3$)$_3$, b Am(L2)(NO$_3$)$_3$, and c Am(L3)(NO$_3$)$_3$. d Nalewajski-Mrozek (N-M) Bond Order Analysis of ML(NO$_3$)$_3$ (M=Am(III), Eu(III); L=L1, L2, L3). e Energy decomposition analysis of the total bonding interaction between fragments M(NO$_3$)$_3$ and ligand in ML(NO$_3$)$_3$ (M=Am(III), Eu(III); L=L1, L2, L3). f Calculated Gibbs free energies ($\Delta G$) of the complexation reactions and the difference in $\Delta G$ between Am(III) and Eu(III) ($\Delta \Delta G$) in nitrobenzene. g Frontier molecular orbital energy level diagram of L1, L2, and L3 fragments in Am(L)(NO$_3$)$_3$. The envelope of HOMO and LUMO is given with contour values of 0.02 a.u. h The design strategy of the optimal extractant screened by DFT calculation.

To evaluate the differences in M-L chemical bonding between Am(III) and Eu(III) for each ligand and deeply explore the nature of these bonds, we performed a detailed bonding analysis on ML(NO$_3$)$_3$ complex, including bond orders, energy decomposition analysis (EDA) and...
natural orbitals for chemical valence (NOCV). The calculations are summarized in Tables S3-S5 and Fig. S5-S16.

The results of the bond order analysis (Fig. 1d and Table S4) show that the bond orders for M-O and M-N with Am(III) are greater than those with Eu(III) among the three ligands. This suggests that the ligands have a stronger binding ability with Am(III) compared to Eu(III). Moreover, the EDA results (Fig. 1e) show that Am(III) complexes have more negative total bonding energies than Eu(III) complexes, which also indicates a stronger binding affinity of the ligands towards Am(III). To further explore the causes behind these differences, we have compared the various components in the EDA results (Table S5). The detailed analysis reveals that Am(III) complexes are more favorable in terms of electrostatic stabilization compared to Eu(III) complexes. However, this interaction was offset by Pauli repulsion energies. Hence, summing these two energies (steric interaction) resulted in small negative values (ranging from -0.44 to -7.03 kcal·mol⁻¹) for all the complexes, with more negative values observed in the Eu(III) complexes. Considering only these two metrics, one would predict that the Am(III) complexes would not be stable compared to Eu(III) complexes. Nevertheless, significant negative stabilization energies were obtained once the orbital interaction terms were considered. Subsequently, to further understand the orbital interactions in the complexes, we analyzed the M–O and M-N bonding interactions using ETS-NOCV method (Fig. S5-S16). The NOCV deformation densities show that the interactions between the metals and the ligands in all complexes are dominated by σ-bonds. These primarily σ-bonding interactions consisted of O 2p- orbitals and N 2p- orbitals mixing with 4f-/5f-, 5d-/6d-, and 6s-/7s- orbitals of the metals. Compared to the f (4f/5f) orbitals, the d (5d/6d) orbitals contribute more to the metal-ligand bonding. Consistent with the results of literatures⁴¹-⁴⁷, d orbitals are more diffuse compared to the more contracted f orbitals, resulting in differing bonding capabilities.

In general, the bonding analysis of ML(NO₃)₃ complexes reveals that compared to Eu(III), the three ligands have a stronger binding affinity with Am(III), suggesting that all these designed ligands may possess certain separation capabilities towards Am(III) and Eu(III). It is worth mentioning that, within the same metal complex, the larger bond orders of M-O
compared to M-N also suggest that introducing O coordination can enhance the extraction
capability of the ligand, which is consistent with the experimental experience and further
demonstrates the accuracy of our calculations.

In order to identify the most promising extractants for separating Am(III) and Eu(III),
thermodynamic calculations were performed on the ML-type complexes by model reaction (1),
which was generally employed in the literatures.

\[ [\text{M(NO}_3\text{)(H}_2\text{O})_8]^{2+} + \text{L} + 2\text{NO}_3^- = \text{ML(NO}_3\text{)_3} + 8\text{H}_2\text{O} \]  (1)

Based on the most stable conformations of the complexes (is1) and ligands (CI) (Fig. S17
and Table S7), we calculated the Gibbs free energies (\(\Delta G\)) of the reactions and the difference
in \(\Delta G\) between Am(III) and Eu(III) (\(\Delta \Delta G\)) (Fig. 1f and Table S8). The calculated Gibbs free
energies (\(\Delta G\)) show that the extraction capabilities of the three ligands for the metals Am(III)
and Eu(III) are \(\text{L}_3 > \text{L}_2 > \text{L}_1\). Additionally, the calculated \(\Delta \Delta G\) values of -0.77, -3.12, and -
3.73 kcal\cdot mol\(^{-1}\) for \(\text{L}_1\), \(\text{L}_2\), and \(\text{L}_3\), respectively, also indicate that their separation capabilities
follow the same order: \(\text{L}_3 > \text{L}_2 > \text{L}_1\). Ultimately, the highest occupied molecular orbital
(HOMO) and the lowest unoccupied molecular orbital (LUMO) frontier molecular orbitals of
ligand fragments in complexes were analyzed, with the results shown in Fig. 1g and Fig. S18.

The results indicate that the frontier molecular orbital energies of \(\text{L}_1\) and \(\text{L}_2\) fragments are
quite similar. However, compared to \(\text{L}_1\) and \(\text{L}_2\), \(\text{L}_3\) exhibits a significantly lower LUMO
energy level, making it easier to accept electrons from the metals. As such, \(\text{L}_3\) is preliminarily
identified as the most promising ligand for the extraction of Am(III) and Eu(III).

The above theoretical studies predicted the extraction and separation capabilities of the three
designed ligands, demonstrating the importance of theoretical design in the development of
extractants. The computational results all indicate that \(\text{L}_3\) has the strongest extraction and
separation capabilities. This allows us to preliminarily predict that \(\text{L}_3\) could potentially be a
promising extractant for separating Am(III) and Eu(III) (Fig. 1h). Consequently, we
synthesized \(\text{L}_3\), along with \(\text{L}_1\) and \(\text{L}_2\) for comparison, and carried out the corresponding
extraction experiments to develop the next-generation An(III)/Ln(III) separation extractant and
confirm the critical role of computational insights in advancing separation chemistry.
Synthesis of Extractants via a \textit{de novo} Construction Method

The synthesis methods of intermediate 1 (8-amino-7-formylquinoline-2-carbonitrile), intermediate 2 (N-ethyl-2-oxo-N-(p-tolyl)propanamide), intermediate 5 (3,3,6,6-tetramethylcyclohexane-1,2-dione) and \( L_3 \) extractant are shown in Fig. 2. The synthesis methods of extractants \( L_1 \) and \( L_2 \) extractants for comparison are shown in Fig. S1. The \(^1\)H and \(^{13}\)C NMR spectra of the intermediate 1, intermediate 2, and intermediate 5 are shown in Fig. S19-S24. The \(^1\)H NMR spectra, \(^1\)H-\(^1\)H COSY and NOESY NMR spectra, ESI-MS results, and organic elements analysis results of \( L_1 \), \( L_2 \), and \( L_3 \) extractants are shown in Fig. S25-S31 and Table S8.
Using 7-methylquinoline as the starting material, acyl and amino groups can be introduced at positions 7 and 8 in intermediate 1 through multiple steps of substitution, oxidation and reduction reactions. These two functional groups could provide coupling sites for the subsequent construction of the phenanthroline skeleton. Simultaneously, the carbonitrile group at position 2 serves as a reaction site for the subsequent generation of diamide dihydrazide and further cyclization reactions to form triazines side chains. The raw material with simple structure (pyruvate, oxaloyl chloride and N-ethyl-4-methylaniline) were dissolved and mixed...
to obtain intermediate 2 under mild conditions (room temperature) with a yield of 63%. The synthesis method of intermediate 5 referred to a previous literature\textsuperscript{20}. By strictly controlling reaction conditions and manipulation, we succeeded in obtaining the products with a higher yield than that reported in the literature\textsuperscript{20}.

In the synthesis of \textbf{L3} extractant, we abandoned the conventional strategy of functionalizing substituents directly onto the phenanthroline framework and instead pioneered a \textit{de novo} construction of the phenanthroline skeleton based on the Friedländer reaction, achieving a high yield of 76\%\textsuperscript{48}. Furthermore, since intermediate 2 was synthesized beforehand, the amide side chain was successfully linked to the phenanthroline skeleton, thereby avoiding additional experimental steps. Additionally, the subsequent triazine cyclization reaction conditions were relatively mild and did not involve strong acids or metal catalysts, preventing hydrolysis of the amide side chain.

To date, most phenanthroline derivatives extractants were synthesized through grafting the functional groups onto the parent phenanthroline skeleton. There are some disadvantages such as poor reaction selectivity, easy decomposition of intermediates and low yield of end products, particularly difficult to construct unsymmetrical extractants. In this work, the phenanthroline skeleton in \textbf{L3} extractant was readily afforded using an Friedländer reaction between intermediate 1 and intermediate 2 in one step with a high efficiency, which is an effective method for constructing phenanthroline-derived derivatives. Due to its universality and versatility, by changing the structure of intermediates 1, 2 and 5, a vast of phenanthroline-based extractants with different structures can be modularly constructed, thus providing a solution for the development of highly efficient extractants.
Extraction and Separation Performance

Fig. 3. Extraction, separation and stripping performances of L1/L2/L3. The influence of solution acidity ([HNO₃] = 0.1-4.0 M, [L] = 20 mM) on the Am(III)/Eu(III) extraction by a L1, b L2, and c L3; d The distribution ratio of Am(III) and Ln(III) extracted by L3 ([HNO₃] =2.0 M, [L] = 20 mM); e The influence of extractant concentration ([L] = 2-20 mM, 3 M HNO₃) on the Am(III)/Eu(III) extraction by L3; f The Am(III) stripping efficiency of dilute nitric acid for L3.

Initially, ²⁴¹,²⁴³ Am(III) and ¹⁵²,¹⁵⁴ Eu(III) served as representative species for An(III) and Ln(III), respectively, to assess the extraction and separation performance of the extractants. As anticipated, the L3 extractant exhibits an outstanding extraction and separation capabilities for Am(III)/Eu(III) across a wide acidity range with $D_{\text{Am(III)}} = 28-44$ and $SF_{\text{Am(III)/Eu(III)}} = 51-57$ (Fig. 3c). The peak distribution ratios for Am(III) and Eu(III) are attained at 2 M HNO₃.

Compared to L1 and L2 (Fig. 3a and 3b), L3 obviously exhibits a stronger extraction affinity towards Am(III) ($L_3 > L_1 > L_2$). The Am(III)/Eu(III) separation ability follows the order of $L_3 > L_2 > L_1$ and indicates that the separation ability of L2 and L3 extractant with bipyridine and phenanthroline skeletons can be improved with an increasing number of N donor atoms, which is consistent with the DFT calculation results. Such superior performance of L3 stems from the preorganized phenanthroline skeleton, which maintains the extractant configuration and prevents conformational reversal during metal ion coordination. Additionally, the presence of the electron-rich O donor atom in the amide side chain enhances the extraction capability,
while the softer N donor atom in the triazine side chain significantly improves Am(III)/Eu(III) selectivity. These three attributes synergistically boost the extraction and separation effect of the L3 extractant for Am(III)/Eu(III).

Besides Eu(III), the spent fuel solution contains other Ln(III) elements like Gd(III) and Sm(III), requiring proper separation alongside Eu(III). Remarkably, the L3 extractant demonstrates nearly no extraction capability for all Ln(III) species, implying exceptional group selectivity for An(III) and Ln(III). The $D_{\text{Ln(III)}}$ values do not exceed 0.2 at 1-2 M HNO$_3$, and even decrease below 0.1 under the high acid condition of 4 M HNO$_3$, achieving an extremely high $SF_{\text{Am(III)/Ln(III)}}$ value over 280 (Fig. 3d and Table S10). The L3 extractant overcomes the common issue of strong co-extraction of light Ln(III) by DAPhen extractants, facilitating complete separation between An(III) and Ln(III)$^{27}$.

The slope analysis method was utilized to determine the quantity of extractant molecules in the extracted complex. Fitted slopes between L3 and Am(III)/Eu(III) yield values of 1.84 and 1.45, respectively (Fig. 3e), indicating the potential generation of both ML and ML$_2$ types of extracted complexes concurrently. In addition, the proportion of ML$_2$-type extracted complex formed by L3 and Am(III) is higher than that with Eu(III). This disparity may be attributed to the stronger binding affinity of L3 with Am(III) compared to Eu(III), leading multiple extractants to preferentially coordinate with Am(III).

In practical application, dilute nitric acid is favored as a stripping agent due to its low cost, easy preparation, and lack of interfering ions. The L3 extractants were tested using dilute nitric acid of varying concentrations to assess Am(III) stripping efficiency (Fig. 3f). Remarkably, lower nitric acid concentrations significantly enhance stripping efficiency, consistent with the extraction trend. By employing 0.001 M HNO$_3$ as the stripping agent, the cumulative three-stage stripping efficiency of L3 reaches 92.72%. It is anticipated that employing more stages would yield a higher stripping efficiency. For BTPhen extractants, water-soluble ligands such as TEDGA need to be used as the stripping agent to achieve similar stripping effects, which undoubtedly increases the difficulty of the operation process and subsequent treatment$^{49}$.

To facilitate the next-generation development of a practical An(III)/Ln(III) separation process, we propose that the L3 extractant addresses several critical considerations in this field. Specifically, the extractant should exhibit robust capabilities for the extraction of Am(III) and
the subsequent separation of Am(III) from Ln(III) ions. Moreover, it is essential that the extractant does not extract any Ln(III) ions over a wide range of acidity levels. Furthermore, the target Am(III) ions should be efficiently stripped using dilute nitric acid as the stripping agent. Given that the L3 extractant is the only known candidate capable of simultaneously fulfilling these requirements, we assert that it holds significant application value and represents a pivotal choice for the advancement of Am(III)/Ln(III) separation processes in the future.

**Coordination Modes in the Solution System**

Fig. 4. Coordination mechanisms of Ln(III) and L3 in the solution system. a Stacked ¹H NMR titration spectra of La(III) and L3 (■ = ligand peaks; ◆ = 1:1 complex peaks; ▲ = 1:2 complex peaks); b ¹H-¹H COSY NMR spectra of La(III) and L3 complex; c UV-Vis spectra, d Species fraction with increasing equivalents.
of Eu(III) with \textbf{L3} during UV-Vis spectroscopic titration, and \textbf{e} Molar absorptivity of ligands and complexes
(up: theoretical predicted results, down: experimental fitted results); Dominant orbital character of \textbf{L3}, \textbf{g}
Eu(\textbf{L3})(\text{NO}_3)_3, \textbf{h} [Eu(\textbf{L3})_2\text{NO}_3]^{2+} associated with electronic transitions. The contour value is 0.02 a.u.

Slope analysis reveals that \textbf{L3} can generate two complexes, M:L = 1:1 and 1:2 with Am(III) and Eu(III), a finding well supported by \textsuperscript{1}H NMR titration\textsuperscript{50}. A comprehensive analysis of Fig. 4a and Fig. S32 indicates that peak intensity in the aromatic region of \textbf{L3} gradually diminishes with Ln(III) addition. New peaks (▲) continuously emerge, with intensity peaking in the M/L = 0.4-0.5 range, indicating initial formation of ML\textsubscript{2} complex. With further Ln(III) addition, ML\textsubscript{2} complex peak diminishes, replaced by a peak group (●) representing ML complex dominance at M/L=2.0. Two-dimensional NMR analysis (\textsuperscript{1}H-\textsuperscript{1}H COSY and \textsuperscript{1}H-\textsuperscript{1}H NOESY) of the La(III)-\textbf{L3} system at the titration end point reveals the coupling relationship of adjacent hydrogen atoms in the formed complexes and the spatial interaction between them. Fig. 4b show that the chemical shifts of benzyl hydrogen (No.7 and No.8) in \textbf{L3} are more similar after coordination, which proves that the electron cloud density on the benzene ring is reduced and the coupling effect is stronger. The \textsuperscript{1}H-\textsuperscript{1}H NOSEY spectrum cannot observe cross peaks beyond the diagonal, indicating the absence of adjacent hydrogen atoms less than 4.5 Å apart (Fig. S33). This shows that the complex is uniformly dispersed in the solution system, and there is no agglomeration behavior caused by hydrogen bond and charge attraction.

The mass spectrometry study further confirmed that Eu(III) and \textbf{L3} can form a variety of complexes with stoichiometric ratios of 1:1 and 1:2 in the gas phase, whose structures are [Eu(\textbf{L3})(\text{NO}_3)_2]^+, [Eu(\textbf{L3})_2(\text{NO}_3)_2]^{2+} and [Eu(\textbf{L3})_2(\text{NO}_3)_2]^+, respectively (Fig. S34). The UV-Vis absorption spectra of the solution coordination system involving Ln(III) and \textbf{L3} were recorded using a UV-Vis spectrophotometer and analyzed using the \textit{HypeSpec} program to ascertain coordination species, stability constants, and species fraction curves throughout the coordination process\textsuperscript{51,52}. Due to the presence of aromatic color groups (phenanthroline, triazine and tolyl), \textbf{L3} exhibit distinct absorption spectra in the UV region, allowing Eu(III) to be used as a titrant for studying their coordination mode and ability. Fig. 4c shows that with the continuous addition of Eu(III), the absorption peak of \textbf{L3} at 289.0 nm gradually decreases and is replaced by two new absorption peaks at 254.6 and 311.6 nm. It is fitted that the log $\beta$ values of Eu(\textbf{L3})\textsuperscript{3+} and Eu(\textbf{L3})\textsubscript{2}\textsuperscript{3+} complexes are 6.66 and 11.73, respectively (Fig. 4d). Eu(III)
and **L3** can simultaneously form ML and ML$_2$ complexes, indicating a positive correlation between molar absorbance of complexes and the number of participating ligands in coordination process (Fig. 4e).

To deeply understand the nature and causes of the trend in spectral peak changes observed in the experiments, time-dependent density functional theory (TDDFT) calculations were performed for the **L3**, EuL$_3$(NO$_3$)$_3$ and [Eu(L$_3$)$_2$NO$_3$]$^{2+}$, all of which have available experimental UV-Vis spectra data (Fig. S35-S37 and Tables S11-S13). The simulated UV-Vis spectra are consistent with the trend observed in the UV-Vis titration experiments, that is, the absorption peaks of the complexes show a slight redshift when compared to those of the free ligands. Moreover, this red shift trend becomes more pronounced as the coordinated number of ligands increases. Further analyses of electronic transitions reveal that, in addition to ligand-to-ligand charge transfer (LLCT), the intense transitions in the complexes can also be assigned to ligand-to-metal charge transfer (LMCT), i.e., ligand → 4f, when compared to the free ligand. These LMCT transitions are likely the reason for the redshift in absorption peaks. Additionally, the UV-Vis spectra for the corresponding Am(III) complexes were also calculated to compare with those of Eu(III) complexes (Fig. S38-S41 and Tables S14, S15). The results show that the spectra of Am(III) complexes display a slight redshift and the intense transitions associated with the metal can be assigned to LMCT, i.e., ligand → 5f, and metal-to-ligand charge transfer (MLCT), i.e., 5f → ligand. However, within the same spectral energy range, there are no transitions from 4f → ligand in Eu(III) complexes. This is due to the energy of the occupied 4f orbitals is much lower than the 5f orbitals, which means transitions from the 4f orbitals to the ligand orbitals require more energy. These computational results reveal the distinct behaviors of the 5f and 4f orbitals during electron transitions, and further validate the conclusions drawn from the experimental spectra.

The fluorescence effect of Eu(III) in solution enables the investigation of its fluorescence characteristics during coordination reactions with ligands, shedding light on coordination thermodynamics and complex structure. Each peak in the fluorescence spectrum corresponds to an electron transition of Eu(III) (594 nm, $^5$D$_0$→$^7$F$_1$; 616 nm, $^5$D$_0$→$^7$F$_2$; 650 nm, $^5$D$_0$→$^7$F$_3$; 683 and 704 nm, $^5$D$_0$→$^7$F$_4$). Unlike other phenanthroline-based extractants, the addition of **L3** decreases the fluorescence intensity of Eu(III) (Fig. S42). This may be attributed to the
significant difference between the trilinear state energy level of the phenanthroline skeleton and triazine side chains and the $^5D_0$ level of rare earth, preventing energy conversion to Eu(III). The stability constants of the complexes formed by $\text{L}_3$ and Eu(III), Eu($\text{L}_3$) and Eu($\text{L}_3)_2$, are 6.61 and 11.87, respectively, slightly higher than the data obtained by UV-Vis absorption spectroscopy, which can be considered a reasonable deviation caused by different methods (Table S16).

Crystal Structures of Complexes in the Solid State

Fig. 5. Single-crystal structures of Eu(III) complexes formed with $\text{L}_3$. a The single-crystal structure, b coordination mode of Eu(III) ion, and c stacking mode of Eu($\text{L}_3$)(NO$_3$)$_3$ complex; d The single-crystal structure, e coordination mode of Eu(III) ion, and f stacking mode of [Eu($\text{L}_3$)$_2$(ClO$_4$)]·(ClO$_4$)$_2$ complex.

The X-ray single-crystal diffraction is considered as an efficient method for obtaining the structural information of ligands and complexes in the solid-phase. Crystals of complexes with different stoichiometries of $\text{L}_3$ and Eu(III) were obtained, revealing their structures, coordination modes, and packing patterns as depicted in Fig. 5, with average bond lengths shown in Table S17.

Crystals of two distinct complexes for Eu(III) and $\text{L}_3$, Eu($\text{L}_3$)(NO$_3$)$_3$ and [Eu($\text{L}_3$)$_2$(ClO$_4$)]·(ClO$_4$)$_2$, were obtained through a solvent diffusion method. Different from CyMe$_3$-BTPhen extractants, the triazine side chain configuration of $\text{L}_3$ involved in coordination is the same as that of ligand crystal, which avoids the energy barrier required to
overcome due to the conformation inversion of ligand during coordination\textsuperscript{20}. In both complexes, \textbf{L3} engages in coordination with Eu(III) ions in a tetradentate chelating manner\textsuperscript{55}. However, the coordination patterns differ noticeably. In Eu(\textbf{L3})(\text{NO}_3)_3, the phenanthroline skeleton in \textbf{L3} flips to the same side when coordinating with Eu(III), with its two N donor atoms on the phenanthroline skeleton alongside the triazine (N)/amide (O) side chains participating in coordination (Fig. 5a). Concurrently, three nitrate ions coordinate with Eu(III) in a bidentate mode, providing additional coordination atoms while neutralizing the positive charge of the complex (Fig. 5b). Ten donor atoms coordinate with Eu(III) simultaneously, showing slight differences in average bond lengths (Table S17): Eu-O(amide)(2.42 Å) < Eu-O(\text{NO}_3^-)(2.50 Å) < Eu-N(phen)(2.56 Å) ≈ Eu-N(triazine)(2.57 Å). Fig. 5e illustrates that the distance between phenanthroline skeletons in two near complexes is 3.40 Å, leading to a relatively strong π-π stacking interaction\textsuperscript{56}. Conversely, when the anion is the weaker coordinating ClO\textsubscript{4}^-, the second \textbf{L3} ligand can readily participate in coordination (Fig. 5d), which is similar to the tetradentate phenanthroline-derived phosphonate ligands\textsuperscript{57}. Only one ClO\textsubscript{4}^- acts as an ancillary ligand for coordination and charge neutralization, with the remaining charge being balanced by free ClO\textsubscript{4}^- anions. In [Eu(\textbf{L3})_2(ClO\textsubscript{4})](ClO\textsubscript{4})_2, Eu(III) exhibits a coordination number of 9, contributed by two \textbf{L3} ligands and one ClO\textsubscript{4}^- (Fig. 5e). This could be attributed to the larger volume of ClO\textsubscript{4}^-, hindering the formation of a 10-coordinate complex. However, due to the larger volume of [Eu(\textbf{L3})_2(ClO\textsubscript{4})](ClO\textsubscript{4})_2, it cannot form extensive offset face-to-face π-π interactions, relying instead on tilted edge-to-face π-π interactions between the phenanthroline and toluene moieties on the side chain of another ligand (Fig. 5f).

Given the unavailability of a single crystal structure of 1:2 complex of \textbf{L3} in nitric acid solution, we performed DFT calculations on the [M(\textbf{L3})_2NO\textsubscript{3}]\textsuperscript{2+} (M=Am(III), Eu(III)) complexes to gain detailed structural insights on the molecular level (Fig. S43-S45 and Tables S20, S21). In these optimized complexes, two \textbf{L3} molecules coordinate with Am(III)/Eu(III) in a tetradentate chelate form, complemented by an additional nitrate anion participated as a bidentate ligand, yielding a coordination number of 10.

In summary, to overcome the inherent limitations of existing An(III)/Ln(III) separation extractants in simultaneously achieving extraction, stripping, and separation performances, we employed DFT calculations to assist in screening out a novel class of unsymmetrical
phenanthroline-derived extractants with potential An(III)/Ln(III) separation capabilities. Subsequently, an unexampled de novo synthetic approach was developed to construct this optimal extractant with pre-organized phenanthroline skeleton efficiently. Due to its universality and versatility, by simply adjusting the structure of intermediates, a vast of phenanthroline-based extractants with desired structures could be modularly constructed, thus providing a solution for the development of highly efficient extractants. As anticipated by DFT results, the Et-Tol-CyMe₄-ATPhen extractant demonstrated a highly efficient Am(III) extraction and negligible Ln(III) extraction, achieving an extremely high separation factor of Am(III) and Ln(III) \( (D_{\text{Am}} > 40, SF_{\text{Am(III)/Ln(III)}} > 280) \). Meanwhile, Am(III) could be fully stripped by using the most convenient dilute nitric acid as the stripping agent. The systematic spectroscopic analysis using \(^1\)H NMR, ESI-MS, UV-Vis absorption, and fluorescence spectroscopy elucidated that the Et-Tol-CyMe₄-ATPhen coordinated Ln(III) in two complexes with \( \log \beta_1 = 6.41 \pm 0.02 \) and \( \log \beta_2 = 11.73 \pm 0.05 \). Finally, single-crystal structures of Eu(III) complexes with different stoichiometric ratios (Eu(L₃)(NO₃)₃ and [Eu(L₃)₂(ClO₄)]⁻(ClO₄)₂) facilitated a molecule-level understanding of the coordination mode of L₃ with f-block elements. The unsymmetrical extractant developed in this work holds the capability required to discern subtle chemical distinctions between An(III) and Ln(III), overcoming the current challenges in An(III)/Ln(III) separation. Consequently, this work provides an ideal candidate for the next-generation extractant in An(III)/Ln(III) separation.

**Methods**

**DFT Computational Details**

Kohn-Sham density functional theory (DFT) calculations were performed on the following molecules\(^57\): L₁, L₂, L₃, ML(NO₃)₃ (M= Am(III), Eu(III); L=1,2,3) and [M(L₃)₂NO₃]²⁺ (M= Am(III), Eu(III)). Geometry optimizations were performed by employing the hybrid functional PBE0 as implemented in the Gaussian 16 program\(^60,61\). For Eu(III) and Am(III), the ECP28MWB/ECP28MWB-SEG\(^62,63\) and ECP60MWB/ECP60MWB-SEG\(^64,65\) basis sets and pseudopotentials were applied, respectively. For nonmetal atoms, the def2-TZVP basis sets\(^66\) (L and ML-type complexes) and the 6-311G\(^*\) basis sets\(^67\) (ML₂-type complexes) were applied,
respectively. For each molecule, solvation effects were evaluated using the SMD solvation model with def2-TZVP basis sets for nonmetals and previously mentioned pseudopotentials and basis sets for metals. Further, time-dependent density functional theory calculations with PBE0 functional (TDDFT/PBE0) were performed on the L3, M(L3)(NO3)3 and [M(L3)2NO3]2+ (M = Am(III), Eu(III)) using 6-311G* basis sets for nonmetals.

The chemical bonding analysis of ML(NO3)3 complexes, including bond-order analyses, energy decomposition analysis (EDA) and natural orbitals for chemical valence (NOCV), were performed at the above optimized geometries using PBE functional, scalar relativistic ZORA Hamiltonian, and uncontracted slater-type orbital (STO) basis sets with the quality of triple-ζ plus two polarization functions (TZ2P) implemented in the Amsterdam Density Functional (ADF 2020.103). To balance computational accuracy and computational cost, small-core TZ2P basis sets were employed for all atoms in the bond order calculations, with the frozen core approximation applied to the inner shells [1s2 - 5d10] for Am(III), [1s2 - 4d10] for Eu(III), [1s2] for C, N, and O. In the EDA calculations, all-electron TZ2P basis sets were used for all atoms.

**Solvent Extraction and Stripping Experiments**

*Caution: The Am(III) feed liquid in the radioactivity experiment was a mixture of 241Am(III) and 243Am(III), and the Eu(III) feed liquid was a mixture of 152Eu(III) and 154Eu(III). Relevant experiments were carried out in the professional radiochemistry laboratory at Tsinghua University.*

Firstly, the extractants were dissolved in 1-(trifluoromethyl)-3-nitrobenzene to prepare a solution with a concentration of 2-20 mM as the organic phase in the extraction. The radioactive elements Am(III) and Eu(III) (trace amount) or non-radioactive lanthanide nitrates (0.1 mM) were added to the nitric acid solution with a concentration of 0.1-4.0 M, respectively, as the aqueous phase in the extraction. During the extraction experiment, 1 mL of aqueous phase and organic phase were added to the centrifuge tube, and the magnetic stirrers were used to fully mix the two phases (300 rpm, 60 min). After the extraction reached the equilibrium state, the mixture was centrifuged for phase separation (3000 rpm, 3 min). In the radioactive extraction experiment, 100 µL aqueous phase solutions containing Am(III) and Eu(III) were added to the liquid scintillation (LSC) bottle with LSC cocktail (Ultimate gold, PerkinElmer) and mixed
intensively. The radioactive activity of Am(III) and Eu(III) in aqueous phase before and after extraction were measured by ultra-low level scintillation counter (Quantulus 1220, PerkinElmer). The ICP-OES (iCAP-PRO, Thermo Scientific) was used to measure the concentration of Ln(III) in the aqueous phase before and after extraction. The calculation methods of distribution ratio ($D$) and extraction efficiency ($E$) to Am(III)/Eu(III) and Ln(III) (difference subtraction method) are presented in Supporting Information (Equation S1 and S2).

The slope analysis method was used to identify the chemical composition of extracted complexes and the corresponding calculation equations are shown in Supporting Information (Equation S4 to S9).

The aqueous solutions of 0.1, 0.01, 0.001 M HNO$_3$ was selected as the stripping agents. The acidity of Am(III) feed liquid is 3 M HNO$_3$. The concentrations of L3 extractant in the organic phase were 20 mM. Firstly, the organic phases and aqueous liquids were fully contacted to achieve extraction equilibrium. Then, the extracted organic phases and fresh stripping agents were mixed and centrifuged. The extracted organic phase was stripped three times by fresh stripping agents. The volume of organic and aqueous phases was equal in each extraction and stripping steps. The stirring and centrifugation time were 60 min and 3 min, respectively. Based on the measured radioactivity of Am(III) in the feed liquid, extracted organic phase, and stripped aqueous phase, the single and total stripping efficiency ($S\%$) were calculated respectively and the calculation method is presented in Supporting Information (Equation S3).

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Acknowledgment

We are grateful for financial support from the National Natural Science Foundation of China (U2067213, 22076130 and 22206168). Thanks to Dr. Jiyong Liu of the Department of chemistry and Dr. Xiaoyan Xiao of School of materials science and engineering, Zhejiang University for their help in single-crystal experiment.

Author Contributions

Xiaofan Yang: Conceptualization, Investigation, Writing - original draft; Dong Fang: Resources, Methodology; Linjia Chen: Formal analysis, Data Curation; Yaoyang Liu: Resources; Shihui Wang: Visualization; Lei Xu: Validation; Anyun Zhang: Project administration; Jing Su: Validation, Writing - Review & Editing; Chao Xu: Funding acquisition, Resources; Chengliang Xiao: Funding acquisition, Supervision.

Conflict of Interest

The authors declare no conflict of interest.
Additional information

Supplementary information: The X-ray crystallographic coordinates for structures reported in this Article have been deposited at the Cambridge Crystallographic Data Centre (CCDC), under deposition numbers CCDC 2348572, 2348576 and 2348577. The online version contains supplementary material available at XXX.
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