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ORIGINAL ARTICLE

Shape-persistent macrocycles: efficient extraction towards lanthanide and actinide elements

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Abstract The extraction of three shape-persistent aromatic oligoamide macrocycles (cycloaramides) bearing either apolar or polar side chains at the periphery of the rings has been investigated towards some representative lanthanide and actinide ions, and alkali metal ions. The results from the liquid–liquid extraction of lanthanide and thorium ions from aqueous solutions into dichloromethane revealed remarkably high extractability of up to 99% and selectivity over alkali metal cations. The stoichiometry of the complex formed between the macrocycle and Eu^{3+} or Th^{4+} was determined to be 1:1.

Keywords Cycloaramide · Macrocycle · Hydrogen bonding · Lanthanide · Actinide · Extraction

Introduction

Macrocycles based on aromatic oligoamide [1–7] represent a class of host molecules that are capable of complexation towards metal ions via carbonyl oxygen atoms or amide N–H protons [8, 9]. Recently, the one-step condensation reaction of monomeric diamines and diacid chlorides was found to lead to the highly efficient formation of a series of shape-persistent cyclized oligoamide products in yield of 60–80% [10]. Different from ordinary cyclic aromatic oligoamides that are often associated with flexible amide bonds, these macrocycles are backbone rigidified by intramolecular hydrogen bonds with few degrees of conformation freedom, and thus have well-defined cavities containing introverted O atoms [11]. Besides, they also differentiate from crown ethers with respect to shape-persistency [12–14] that features the noncollapsable nature of these cycles. Interestingly, the macrocycles with six aromatic amide residues with their backbones rigidified by three-center hydrogen bonds was able to bind guanidinium (G) ion with nearly exclusive selectivity [15]. Along with the formation of the six residue macrocycle, at elevated temperature, the otherwise unfavourable macrocycle with eight amide residues was also observed in a yield of 23% due to the increased flexibility of the folded precursors [16]. We and Gong have recently proposed a mechanism for the efficient kinetic macrocyclization where the high yields that deviate dramatically from the computated value for a typical kinetically controlled macrocyclization reaction were attributed to the folding conformation enforced by intramolecular hydrogen bonds and remote steric effect of oligomeric precursors [11]. These macrocycles, cyclo[*n*]aramide ($n = 6, 7, 8$, etc.) as we call for simplicity, constitute a large family of aromatic oligoamide macrocycles with internal nano-sized lumen.

Although the hydrogen-bonding preorganized macrocycles of various sizes and conformations have been available so far [10, 11, 16, 17], those with smaller size seem to be more intriguing in terms of metal complexation. Based on the internal diameter of the macrocycle with six aromatic amide residues, namely, cyclo[6]aramide (0.79 nm), it can be envisioned that highly efficient extraction with this cycle towards smaller metal ions such

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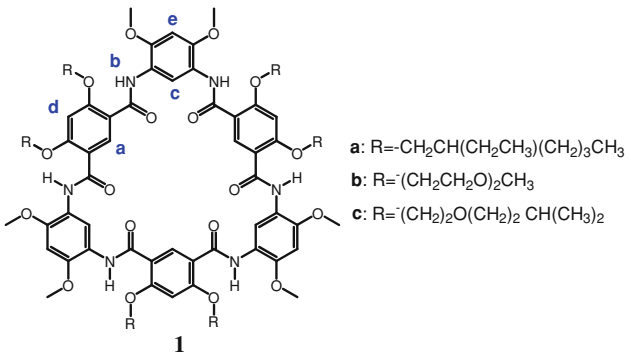
as alkali or alkaline-earth metal ions is expected to be less likely. With its preorganized oxygen atoms that point to the inner cavity, the coordinating sites that resemble those of crown ethers [18–22] make them potential candidates for larger metal ions. However, the binding and extraction of metal ions using the cycloaramides have never been reported before. Herein we report on our findings of the efficient extraction ability of cyclo[6]aramides towards some lanthanide and actinide ions (Scheme 1).

Experimental

UV–vis spectra were measured by SHIMADZU UV-2350. ^{1}H NMR and ^{13}C spectra were recorded on Bruker AVANCE AV II-400 MHz (^{1}H: 400 MHz; ^{13}C: 100 MHz) and Bruker AVANCE AV II-600 MHz (^{13}C: 150 MHz). High resolution mass data were collected by WATERS Q-TOF Premier. All chemicals were obtained from commercial suppliers and were used as received unless otherwise noted. CH_2Cl_2 was dried over CaH_2. The metal salts used were lanthanide and thorium nitrates. They were dried under vacuum for at least 48 h before use and the concentrations of their stock solutions were standardized by complexometry using xylenol orange as coloured indicators [23, 24]. 1,5-Dimethoxy-2,4-diaminobenzene **3** and 2,4-dimethoxy-5-nitroaniline **7** were obtained from reduction of 1,5-dimethoxy-2,4-dinitrobenzene [25]. Diacid chlorides **6** (**a**, **b**, **c**) were prepared from oxalyl chloride and their corresponding diacids, and **4** was synthesized according to similar literature procedures [25]. The stoichiometry of the complex formed between the macrocycle **1a** and Eu^{3+} or Th^{4+} was determined by the method of Job's plot [26].

Synthesis of cyclo[6]aramide **1a**

Diacid chloride **6a**, prepared from hydrogenation of 4,6-bis(2-ethylhexyloxy)isophthalic acid (0.42 g, 1.84 mmol), and diamine **3**, prepared from oxalyl chloride and 1,5-dimethoxy-2,4-dinitrobenzene (0.78 g, 1.84 mmol), were dissolved in CH_2Cl_2 (25 mL) and mixed in the presence of triethylamine (2.2 equiv) at −20 °C. The reaction mixture was stirred and warmed to room temperature over a period of 6 h. After quenching with CH_3OH and removing the solvent, the residue was triturated with CH_3OH and EtOAc. Filtration provided the crude product. Further purification by column chromatography ($CHCl_3$/CH_3OH, 10:1) provided the pure product **1a** (0.58 g, 57.0%). ^{1}H NMR (400 MHz, 40% $CDCl_3$–60%DMSO-d_6) δ: 9.56 (s, 6H, NH), 9.46 (s, 3H, ArH), 9.12 (s, 3H, ArH), 6.83 (s, 3H, ArH), 6.77 (s, 3H, ArH), 4.27 (s, 12H, OCH_2), 3.96 (s, 18H, OCH_3), 2.05 (m, 6H, OCH_2CH), 1.62 (m, 12H, CH_2), 1.53 (m, 12H, CH_2), 1.39 (m, 12H, CH_2), 1.35 (m, 12H, CH_2), 1.00 (t, J = 7.3, 18H, CH_3), 0.90 (t, J = 7.0, 18H, CH_3). ^{13}C NMR (100 MHz, 95% $CDCl_3$–5% CD_3OD) δ: 162.5, 159.9, 146.3, 139.1, 120.5, 118.6, 116.0, 96.0, 95.0, 72.2, 55.8, 39.0, 30.1, 28.9, 23.5, 23.0, 13.9, 10.6. ESI-HRMS (m/z) calcd. for $C_{96}H_{139}N_6O_{18}$ $[M + H]^+$1665.0179; Found 1665.0205.



Scheme 1 Structures of cyclo[6]aramides **1a–1c**

Synthesis of cyclo[6]aramide **1b**

1b was synthesized in a similar procedure to compound **1a** from diacid chloride **6b** and diamine **3**. White solid (0.12 g, 51.1%). ^{1}H NMR (400 MHz, 95% $CDCl_3$–5% CD_3OD) δ: 9.62 (s, 3H, ArH), 9.44 (s, 6H, NH), 9.23(s, 3H, ArH), 6.60 (s, 3H, ArH), 6.51 (s, 3H, ArH), 4.41 (s, 12H, $ArOCH_2CH_2O$), 4.03 (s, 12H, $ArOCH_2CH_2O$), 3.92 (s, 18H, $ArOCH_3$), 3.74 (s, 12H, OCH_2CH_2O), 3.53 (s, 12H, OCH_2CH_2O), 3.33 (s, 18H, OCH_3). ^{13}C NMR (150 MHz, 95% $CDCl_3$–5% CD_3OD) δ: 161.0, 161.9, 159.5, 145.2, 138.8, 120.2, 120.1, 116.3, 115.2, 96.7, 94.3, 71.9, 70.4, 69.0, 68.6, 58.8, 55.8, 29.6. ESI-HRMS (m/z) calcd. for $C_{78}H_{104}N_6O_{30}$ $[M + 2H]^{2+}$ 802.3399; found 802.3402.

Synthesis of cyclo[6]aramide **1c**

1c was synthesized in a similar procedure to compound **1a** from diacid chloride **6c** and diamine **3**. White solid (0.23 g, 61.8%). ^{1}H NMR (400 MHz, 95% $CDCl_3$–5% CD_3OD) δ: 9.50(s, 6H, NH), 9.32 (s, 3H, ArH), 9.27 (s, 3H, ArH), 6.64 (s, 3H, ArH), 6.53 (s, 3H, ArH), 4.40 (t, J = 5.0, 12H, OCH_2CH_2O), 3.98 (t, J = 5.0, 12H, OCH_2CH_2O), 3.93 (s, 18H, OCH_3), 3.58 (t, J = 6.9, 12H, OCH_2), 1.64 (m, 6H, OCH_2CH), 1.45 (m, 12H, OCH_2CH_2), 0.85 (d, J = 6.6, 36H, $C(CH_3)_2$). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 164.8, 164.1, 162.0, 160.2, 159.8, 154.6, 152.4, 136.9, 125.2, 121.0, 115.2, 114.9, 113.9, 96.1, 94.7, 72.2, 71.4, 56.1, 55.6, 39.4, 38.7, 34.3, 34.2, 30.6, 30.0, 28.9, 28.7, 23.9, 23.4, 22.8, 22.7, 14.8, 14.7, 13.8, 11.0, 10.6. ESI-HRMS (m/z) calcd. for $C_{90}H_{128}N_6O_{24}^{2+}$ $[M + 2H]^{2+}$ 838.4490; found 838.4496.

Synthesis of compound **5a**

1,5-Dimethoxy-2,4-dinitrobenzene (0.89 g, 3.88 mmol) was hydrogenated in the presence of 10% Pd/C (88.6 mg) at 0.3 MPa for 8 h at room temperature. The solution was filtered in darkness as fast as possible followed by immediate removal of the solvent. The reduced diamine **3** was used for the immediate coupling reaction. The acid chloride, prepared from 2,4-bis(2-ethylhexyloxy)-5-(methoxycarbonyl)benzoic acid **4** (3.38 g, 7.76 mmol), was dissolved in CH_2Cl_2 (30 mL) and added dropwise to a mixture of the above diamine and Et_3N (1.02 g, 10.08 mmol) in CH_2Cl_2 (20 mL). The solution was stirred at room temperature under N_2 for 7 h. The organic layer was washed with water. Removal of CH_2Cl_2 and trituration with MeOH afforded the product as a white solid **5a** (3.29 g, 84.4%).^{1}H NMR (400 MHz, $CDCl_3$)δ: 9.63 (s, 2H, NH), 9.36 (s, 1H, ArH), 8.90 (s, 2H, ArH), 6.53 (s, 1H, ArH), 6.48 (s, 2H, ArH), 4.11 (m, 4H, OCH_2), 3.97 (m, 4H, OCH_2), 3.88 (s, 6H, OCH_3), 3.85 (s, 6H, OCH_3), 1.98 (s, 2H, OCH_2CH), 1.83 (s, 2H, OCH_2CH), 1.30–1.62 (m, 32H, CH_2), 0.86–0.97 (m, 24H, CH_3).

Synthesis of compound **5b**

A mixture of **5a** (2.15 g, 2.14 mmol) in EtOH (80 mL), KOH (0.52 g, 8.56 mmol) in water (3 mL) was refluxed for 4 h. After cooling to room temperature the reaction mixture was acidified with diluted hydrochloric acid. Removal of most of the organic solvent and filtration provided a white solid **5b** (2.00 g, 95.6%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: δ9.46 (s, 2H, NH),9.14 (s, 1H, ArH), 9.09 (s, 2H, ArH), 6.58 (s, 2H, ArH), 6.46 (s, 1H, ArH), 4.15 (s, 8H, OCH_2), 3.86 (s, 6H, OCH_3), 1.96 (s, 2H, OCH_2CH), 1.84 (s, 2H, OCH_2CH), 1.52 (m, 8H, CH_2), 1.46 (s, 8H, CH_2), 1.33 (d, $J = 3.1$ Hz, 16H, CH_2), 0.97 (m, 12H, CH_3), 0.86 (m, 12H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 164.2, 160.7, 160.4, 160.3, 145.4, 138.0, 119.1, 116.5, 115.4, 109.7, 95.8, 93.5, 71.9, 71.8, 54.7, 38.2, 37.8, 29.3, 29.2, 28.0, 27.9, 22.8, 22.6, 22.0, 21.9, 13.0, 12.9, 10.0, 9.7. ESI-HRMS (m/z) calcd. for $C_{56}H_{84}N_2O_{12}$ K $[M + K]^+$ 1015.5661; Found 1015.5646.

Synthesis of compound **2**

A mixture of compound **5b** (0.50 g, 0.51 mmol), 2,4-dimethoxy-5-nitroaniline **7** (0.22 g, 1.12 mmol), Bop-Cl (0.39 g, 1.53 mmol) and Et_3N (0.21 g, 2.04 mmol) in CH_2Cl_2 (50 mL) was stirred at room temperature under N_2 for 7 h. The organic layer was washed with water and, dried over anhydrous Na_2SO_4 and filtered. Addition of ethyl acetate to the filtrate caused a precipitation, which was filtered to give a yellow solid **2** (2.00 g, 72.2%). ^{1}H NMR (400 MHz, 95% $CDCl_3$–5% CH_2Cl_2) δ: 9.70 (s, 2H, NH, ArH), 9.50 (s, 2H, NH, ArH), 9.20 (s, 2H, ArH), 9.11 (s, 1H, ArH), 9.02 (s, 2H, ArH), 6.57 (s, 1H, ArH), 6.55 (s, 2H, ArH), 6.53 (s, 2H, ArH), 4.14 (d, $J = 6.6$, 8H, OCH_2), 4.03 (s, 6H, OCH_3), 3.93 (s, 6H, OCH_3), 3.89 (s, 6H, OCH_3), 1.97–1.99 (m, 4H), 1.33–1.47 (m, 32H, CH_2), 0.97 (t, $J = 7.3$, 12H, CH_3), 0.89 (m, 12H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 162.2, 162.0, 160.5, 160.1, 153.5, 150.9, 146.8, 137.3, 131.8, 121.4, 120.4, 118.4, 115.8, 115.1, 96.7, 96.1, 95.3, 72.8, 72.5, 56.8, 56.4, 55.9, 53.5, 39.0, 38.9, 30.2, 30.1, 29.0, 28.9, 23.6, 23.5, 23.0, 13.8, 13.7, 10.6, 10.5. ESI-HRMS (m/z) calcd. for $C_{72}H_{101}N_6O_{18}$ $[M + H]^+$1337.7172; Found 1337.7155.

Alkali metal extraction method

The alkali metal picrates were prepared by reaction of picric acid with the appropriate metal carbonate [27]. According to the similar method [28], the extraction experiments from water into dichloromethane were conducted according to the following procedure: an aqueous solution (1.5 mL) containing metal picrate (0.10 mM) and an organic solution (1.5 mL) of ligand **1** or **2** (0.10 mM) were shaken in stoppered glass tube for 1 h at 20 °C to guarantee that the equilibrium could be reached. After separation of the two phases, a 1 mL aliquot of each aqueous layer was transferred to a 5 mL volumetric flask, and the flask was filled to the mark with distilled water. The concentration of the picrate anion remaining in the aqueous phase was determined by UV spectrophotometry at λ_{max} 355 nm. Three independent experiments were carried out. The percentage extraction ($E\%$) was calculated based on the equation: $E\% = 100(A_0 - A)/A_0$, where A_0 is the absorbance of the aqueous solution of a blank experiment in the absence of ligand, A is the absorbance of the aqueous phase after extraction.

Lanthanide and actinide extraction method

According to the reported method [29, 30], 0.10 mM solutions of La^{3+}, Ce^{3+}, Pr^{3+}, Nd^{3+}, Sm^{3+}, Eu^{3+}, Gd^{3+}, and Th^{4+} and a 0.10 mM solution of **1a–c** and **2** in methylene chloride were prepared. 1.5 mL aliquot of each phase was shaken in a stoppered tube for 1 h at 20 °C. The layers were allowed to fully separate. A 0.5 mL aliquot of each aqueous layer and 0.4 mL of 6.4×10^{-4} M Arsenazo(III) solution in sodium formate–formic acid buffer (pH = 2.8) were transferred to a 10 mL volumetric flask, and the flask was filled to the mark with the buffer. The metal concentrations of the aqueous phases were determined by measuring the absorbance of the sample using 665 nm for the actinide solutions and 655 nm for the lanthanide solutions. The extractability of each metal by the ligands was calculated using the following formula:

$$E\% = 100(A_1 - A)/(A_1 - A_0)$$

Where A is the absorbance of the extracted aqueous phase with the Arsenazo(III) indicator, A_1 is the absorbance of the aqueous phase before extraction with the buffer and indicator, and A_0 is the absorbance of metal-free formate buffer and the indicator.

Results and discussion

Three cyclo[6]aramides **1** with both nonpolar and polar side chains were prepared from the diacid chloride of 4,6-dialkoxyisophthalic acid and the diamine reduced from 1,5-dimethoxy-2,4-dinitrobenzene according to the previous similar procedures [10] (Scheme 2). Compared to other side chains employed in macrocyclization for cycloaramides reported, the 2-ethylheptyl group used in this article for **1a** accommodates the solubility of the ligand in most organic solvents. The polar side chains in **1b** and **1c** were used for comparing polarity effect upon extraction from peripheral side chains. Compound **2**, a non-cyclic analogue of **1**, was prepared for comparison via several steps (Scheme 2). All of them were characterized by ^{1}H NMR, ^{13}C NMR and HRMS (Supplementary material).

Liquid–liquid extraction studies

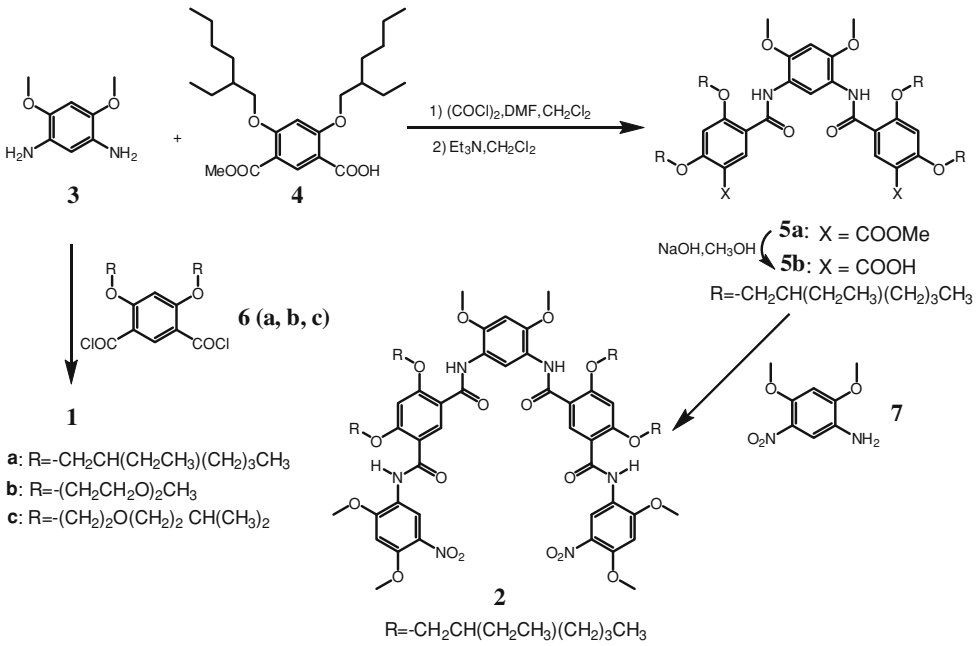
Alkali metal cations

The binding properties of cyclo[6]aramides **1a**, **1b** and **1c** towards alkali metal cations were first examined by the standard picrate extraction method [31]. The results are illustrated in Fig. 1.

The liquid–liquid extraction of all five metal ions followed almost the same trend except Cs^+ but different behavior was observed according to the ligand. For example, **1b** provided the extractability of 66.2% towards extracting Na^+, while **1a** only offered 19.5%. The extractability for **1b** and **1c** for all ions was ca. 60%, around three times that for **1a** except Cs^+. Since the difference between **1a**, **1b** and **1c** lies on the side chains, the increased extractability for **1b** and **1c** suggests the involvement of ether side chains in binding metal ions apart from the capture of cations by the internal cavity of the macrocycles. In contrast to **1a**, the open-chain analogue **2** afforded less than 3% for binding of all metal ions. The very low extraction ability indicated the importance of the structure of the macrocycle where six oxygen atoms are present for binding of alkaline metal ions. Besides, the extractability-independence of **1a** upon ions of different size as seen in small variation of the extractability from Li^+ (17.6%), Na^+ (19.5%), K^+ (21.7%), Rb^+ (19.3%) to Cs^+ (27.2%), indicated the absence of marked selectivity towards alkaline metal ions (Supplementary materials, Table S1).

Lanthanide and actinide

More interesting results using cycloaramides as extractants come from the extraction of lanthanide and actinide as shown in Table 1. The lanthanide ions examined include La^{3+}, Ce^{3+}, Pr^{3+}, Nd^{3+}, Sm^{3+}, Eu^{3+}, Gd^{3+}. Th^{4+} was chosen as the representative ion of actinides in the



Scheme 2 Synthesis of cyclo[6]aramides **1** and its open-chain analogue **2**

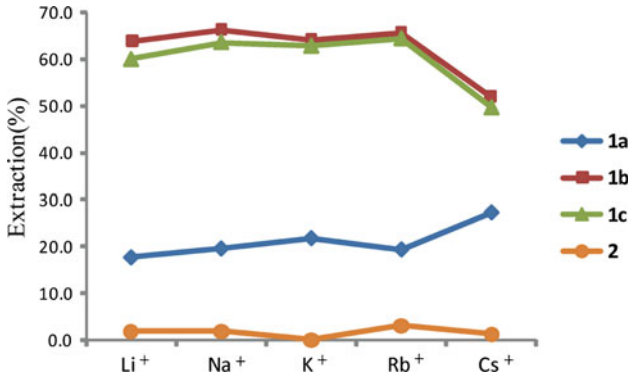


Fig. 1 Extraction of alkali metal nitrates (0.1 mM) by **1a–c** and **2** from water into CH_2Cl_2. Ligand concentration: 0.1 mM

Table 1 Extraction percentage (*E*%) of lanthanide and actinide for **1a–c** and **2** from water into CH_2Cl_2 at room temperature

	1a	1b	1c	2
La^{3+}	92.4	94.4	92.2	25.6
Ce^{3+}	78.4	96.7	88.2	31.2
Pr^{3+}	90.0	96.3	92.4	35.4
Nd^{3+}	93.0	98.1	92.1	56.2
Sm^{3+}	86.3	96.5	93.7	46.9
Eu^{3+}	89.7	98.3	94.3	50.3
Gd^{3+}	92.4	98.7	97.6	55.8
Th^{4+}	97.2	97.9	93.6	46.3

Table 2 Separation factors (SF) of lanthanide and actinide for **1a–c** and **2** from water into CH_2Cl_2 at room temperature

	1a $SF_{Th/M}$	1b $SF_{Th/M}$	1c $SF_{Th/M}$	2 $SF_{Th/M}$
Li^+	162.5	26.5	9.8	47.0
Na^+	143.3	23.8	8.4	44.5
K^+	125.3	26.0	8.7	65.4
Rb^+	145.2	24.4	8.1	27.9
Cs^+	92.9	43.4	14.8	65.4
La^{3+}	2.9	2.8	1.2	2.5
Ce^{3+}	9.6	1.6	2.0	1.9
Pr^{3+}	3.9	1.8	1.2	1.6
Nd^{3+}	2.6	0.9	1.3	0.7
Sm^{3+}	5.5	1.7	1.0	1.0
Eu^{3+}	4.0	0.8	0.9	0.9
Gd^{3+}	2.9	0.6	0.4	0.7

extraction experiment. All macrocycles demonstrated a very high extractability of more than 90% towards lanthanides and Th^{4+}. An exception was Ce^{3+} where it was extracted only in 78.4%. It was noteworthy that the large discrepancy in extracting ability towards alkali metal ions

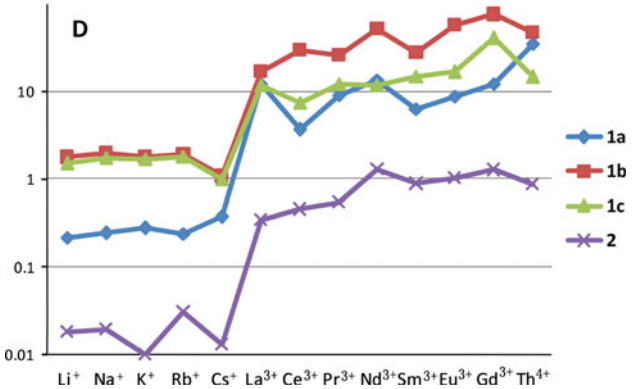


Fig. 2 Distribution coefficients (D) of alkali metal, lanthanide and actinide nitrates (0.1 mM) from aqueous solutions into CH_2Cl_2 containing cyclo[6]aramides **1a–c** and **2** (0.1 mM)

between **1a** and **1b** (or **1c**) due to involvement of ether side chains of **1b** (or **1c**) in complexation was not observed here. Instead, **1a** with non-polar side chains exhibited the same high extraction ability towards all lanthanide and Th^{4+} as **1b** and **1c** with polar ether side chains. Thus, allowing for the fact that the effect of possible complexation of metal ions by peripheral ether side chains was circumvented in **1a**, the above result indicated that the internal chelating sites of six carbonyl oxygens in the macrocycle indeed played a pivotal role in extraction of lanthanide and Th^{4+}. In comparison **2** only afforded extractabilities varying between 25.6 and 56.2%. The lower metal ion affinity may be explained by the mismatched geometrical orientation of oxygens for metal complexation and lack of enough coordinated oxygen atoms in the constructed molecule. The extraction efficiency and separation factors (SF, $SF_{MA/MB} = D_{MA}/D_{MB}$) of these macrocycles and the open-chain analogue **2** towards lanthanide and actinide is also demonstrated in Fig. 2 and Table 2 as compared to those of alkali metal ions.

Among the three macrocycles **1a–1c**, **1a** provided the highest separation factor ranging from 2.6 to 9.6 in terms of thorium with respect to lanthanide elements, while $SF_{Th/M}$ of **1b**, **1c** and **2** are actually comparable (Table 2). This suggested that the macrocycle with non-polar alkyl groups at the periphery of the cycle was inclined to accommodate Th^{4+} better than other metal ions compared to those bearing polar side chains. Macrocycles **1b** and **1c** showed no preference over **2** in separating Th^{4+} from lanthanide ions.

On the other hand, the complexation of **1a** with and Eu^{3+} and Th^{4+} was probed in $CHCl_3$/DMSO (v/v, 95/5) by ^1H NMR experiments. As shown in Fig. 3, the signals from amide protons **b** and aromatic protons **a/c** experienced a significant change upon addition of $Eu(NO_3)_3$. Especially, proton **c** in the presence of Eu^{3+} moved from 9.32 pm of

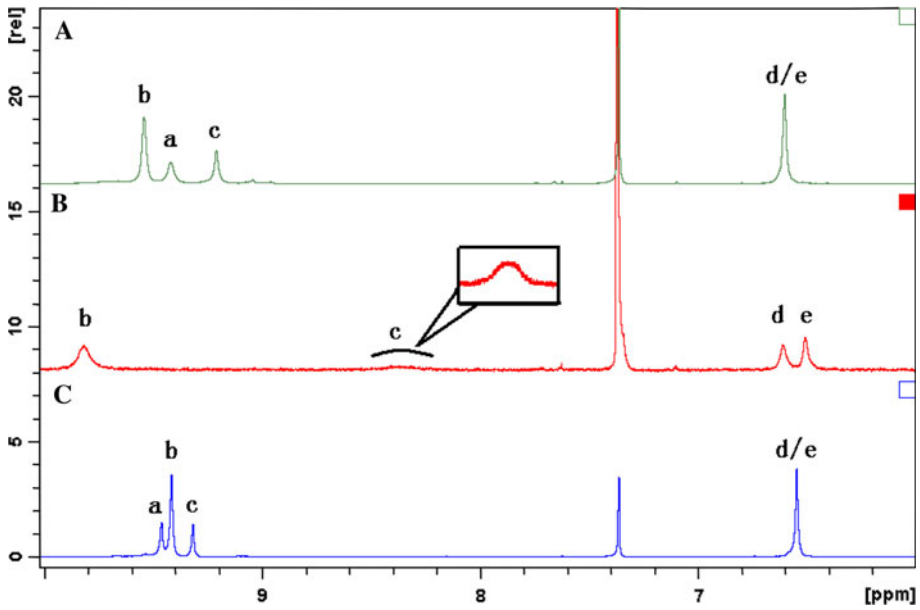


Fig. 3 Stacked plots of partial ^{1}H NMR spectra in 95% $CDCl_3$/5% DMSO-d_6. (**A**) **1a** + $Th(NO_3)_4$ (1:1), (**B**) **1a** + $Eu(NO_3)_3$ (1:1), (**C**) **1a**, 2 mM

free ligand **1a** (**C**) to 8.34 pm of the complex (**B**). Such a tremendous shift is in sharp contrast to that observed in the presence of thorium (**A**), where both protons **a** and **c** only shifted upfield ca. 0.04 and ca. 0.11 ppm, respectively, compared to the free ligand, and proton **b** went downfield ca. 0.14 ppm. These results indicated that the complexation of macrocycles **1a** with lanthanide and actinide thorium did occur by coordinating with internal oxygens of the cycle, which was consistent with the efficient extraction of the macrocycle.

The analysis of the Job's plot versus the concentration of the ligand in the organic phase allowed the determination of the complex stoichiometry. Europium and thorium are found to be 1:1 complex with **1a**. The stability constant of **1a** complex with Eu^{3+} in $CHCl_3$/DMSO (95/5) was determined by ^{1}H NMR titration to be $8.11 \pm 1.51 \times 10^4$ (Supplementary materials, S13–14).

In general, all macrocycles **1a**, **1b** and **1c** are lanthanide and Th^{4+} selective. Macrocycle **1a** with a separation factor of $SF_{Th/Ln}$ 2.9 $\sim$ 9.6 (Table 2) is most effective and more selective for thorium, while the lanthanides are best extracted by **1b**. It seems that the polar ether side chains containing two oxygens in **1b** are more prone to facilitate the distribution between the two phases than the branched ether side chains containing one oxygen atom as shown in **1c**.

Conclusion

In conclusion, liquid–liquid extraction experiments have demonstrated the high binding ability of cyclo[6]aramides towards lanthanides and thorium cations. These aromatic oligoamide macrocycles possess much greater extraction efficiency than its pentameric counterpart. The complexation in the mixed solvent of $CHCl_3$/DMSO (95:5) was evidenced by the change of chemical shift of both amide and internal aromatic protons in ^{1}H NMR spectra. The stoichiometry of the complex formed between the macrocycle and Eu^{3+} or Th^{4+} was determined to be 1:1. The selectivity observed in these macrocycles that differentiate these cations from alkali metal ions makes them potentially useful in separation of lanthanide and actinides from alkali metal ions. With these macrocycles and their derivatives containing a well-defined internal cavity further modification and tuning of the cavity may provide opportunities for finding new extractants for lanthanide and actinides separation.

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