A calixarene-based extractant with selectivity for Am^{III} over Ln^{III}

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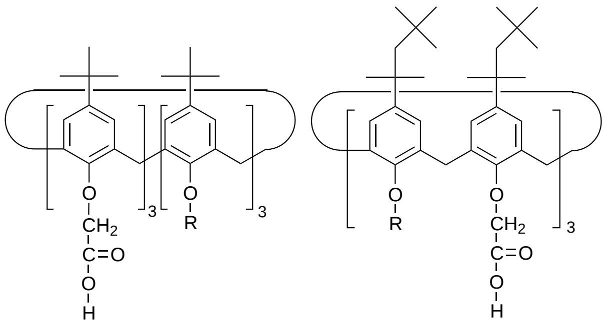
Calix[6]arene-based extractant 4 shows high selectivity and extractability for Am^{III} from weakly acidic solutions due to the cooperativity of different ligating groups.

Among the [1_n]metacyclophane-based ligands[1,2] tested as extractants for metal ions, calix[4]arenes and, to a smaller extent, calix[6]arenes are two of the most popular to date.[3] While calix[4]arenes with ester, amide, carboxylic acid or other monodentate groups can extract alkaline, alkaline earth, several transition and noble metal ions selectively, the larger calix[6]arenes often display a lower selectivity. We previously observed in the case of noble metal extraction that the selectivity can be greatly influenced by the presence of different donor groups, such as CO_2H and amide in a calix[4]arene.[4] Although the mutual separation of lanthanides by calix[4]arenes bearing CO_2H groups is improved by co-extracted sodium ions,[5,6] those ligands have a lower overall extractability towards lanthanides[4] and actinides, such as Am^{III},[7] compared with calix[6]arenes. On the other hand, calix[6]arenes such as ligand **1a**, which serves as a reference compound in the communication, perform as good extractants for Ln^{III} and Am^{III}, but with poor group and mutual separation factors. Conventional extractants such as liquid anion exchangers utilize the concurrent complexation by anions for achieving Ln/Am separation. We now report on the progress in achieving selectivity in the cation exchange-based extraction due to the introduction of mixed monodentate functional groups into calix[6]arenes. The emphasis will be on the relationship between ligand structure and complex formation–extraction.



1a R = CH_2CO_2H
3 R = Me

1b R = CH_2CO_2H
2 R = Me
4 R = $CH_2C(O)NEt_2$

The distribution ratios D ($D = c_{\text{metal, org.}}/c_{\text{metal, aq.}}$) of six selected lanthanide ions Ln^{3+} (Nd, Eu, Tb, Dy, Er, Yb) in the competitive extraction from aqueous into $CHCl_3$ solutions containing ligand **1a** are shown in Fig. 1 on a logarithmic scale as a function of the equilibrium pH. The distribution ratio of Am^{3+} (single element, trace amounts) with ligand **1a** is plotted in the same figure. There is no significant difference in the extractability between Ln^{III} and Am^{III} in these reference systems.

As a first step on the way to improve extractability as well as solubility, we changed *tert*-butyl to *tert*-octyl in the calix[6]arenes.[8] These highly branched ligands are very soluble in low polar organic solvents even without a modifier. The distribution ratios of Am^{III} increase slightly with **1b**, compared with **1a** (Fig. 1). The slope of the plot log D *vs.* pH is 3.0 in accordance to the metal ion charge.

Next, three carboxylic acid groups were introduced alternating with methoxy groups and the extraction into $CHCl_3$ by ligand **2** at 3 mM concentration was studied.§ The extractability decreased significantly [$pH_{0.5}(Am) = 3.3$, $pH_{0.5}(Ln) > 4.5$] due to the smaller number of carbonyl oxygen donor atoms and a less shielded ionophoric cavity, while the selectivity of Am^{III} over Ln^{III} improved, compared with **1b**. The calculated distribution ratios follow the order Am $\gg$ Eu, Nd $>$ Tb $>$ Dy $>$ Yb $>$ Er. The slopes of the plots log D *vs.* pH are lower than 3.0 which may be caused by the co-extraction of an anion in the metal ion coordination sphere.

At this point, we tested the influence of ligand geometry on the selectivity and extractability under the same conditions by using ligand **3**.¶ The extractability was low, with $pH_{0.5}$ being 3.5 for Am, Eu and Nd. The selectivity of Am over Ln at pH $\geqslant$ 3, where more than 10% of Am is extracted, was low due to different slopes of the plots log D *vs.* pH. It thus became clear that the geometrical arrangement of functional groups on the calixarene backbone is a key factor for the separation in the present system.

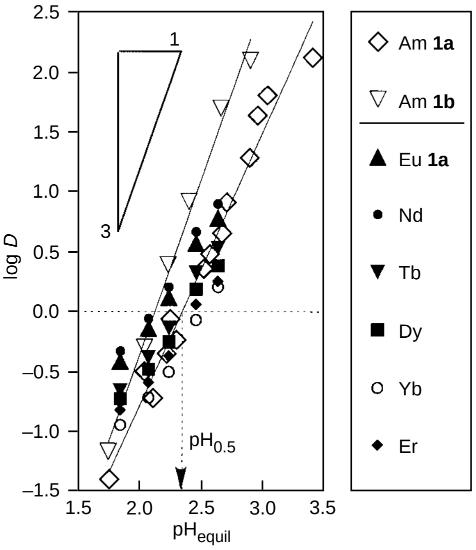


Fig. 1 Distribution coefficients D of trivalent Am and Ln in the extraction from aqueous to $CHCl_3$ solutions at 298 K by ligands **1a** and **1b**. Aq. phase (Am series): $^{241}Am^{III}$ activity 1 kBq ml^{-1} (3.3×10^{-8} M), HNO_3 (various conc.); organic phase (Am series): 5 mM (◇, ▽) ligand, series (◇) contains 2% octan-1-ol as modifier, analysis by liquid scintillation counting of the aq. phase after extraction; aq. phase (Ln series): 0.6 mM $Ln(ClO_4)_3$ (Ln = Nd + Eu + Tb + Dy + Yb + Er, 0.1 mM each), $HClO_4$ (various conc.); organic Phase (Ln series): 3 mM ligand **1a**, 4% octan-1-ol, analysis by ICP-AES of aq. and back-extracted phase (stripping by titriplexIII, mass balance $> 99\%$).

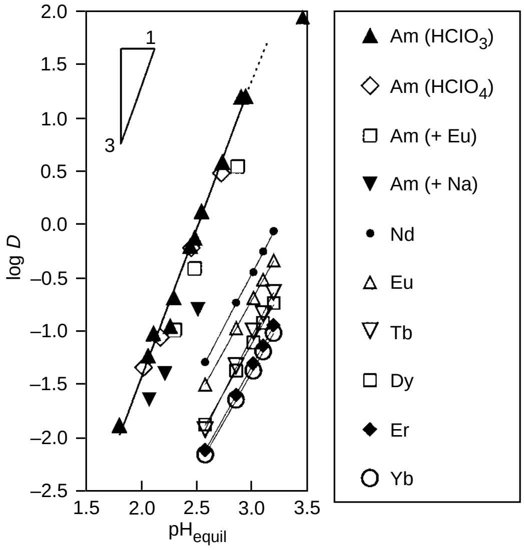


Fig. 2 Distribution coefficients of trivalent Am and Ln for ligand **3**. Aq. phase (Am series): ^{241}Am^{III} (1 kBq ml^{-1}), HNO$_3$ (▲ , ▼) or HClO$_4$ (◇, □), additional 0.3 mM Eu(ClO$_4$)$_3$ or 0.01 M NaNO$_3$ as indicated; aq. phase (Ln series) see Fig. 1; organic phase: CHCl$_3$ containing 3 mM ligand **4**.

In order to improve the extractability (expressed as log *D*), while keeping a good group separation, three amide groups were introduced alternating with three carboxylic acid groups and ligand **4** was obtained, thus avoiding an undesirable excess of ionizable groups over the metal ion charge, but having a sufficient number of carbonyl oxygen donor atoms.|| The results are shown in Fig. 2. The extractability of Am^{III} was high, thereby achieving high selectivity over Ln^{III}. A similar improvement in extraction was previously observed for Pd^{II} and Au^{III} upon substituting excessive CO$_2$H groups by amide groups.[4] The proposed stoichiometry of the extracted complex is 1 : 1 (Am : **4**). The extractability of Am^{III} is still high, when Eu^{III} at a 10^4 times higher or Na$^+$ at a 3×10^5 times higher concentration is present in the aqueous phase.

In conclusion, ligand **4** has an only slightly higher pH$_{0.5}$ value of 2.5 compared with reference ligand **1a** (2.35), but a much higher selectivity over trivalent lanthanides. The separation factors at pH = 3.0 are 66 (Am/Nd) and 118 (Am/Eu). Further studies will deal with competitive extraction of actinides at higher concentrations.

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Footnotes and References

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§ *Synthesis* of **2**: *p-tert*-Octylcalix[6]arenehexaol was treated with K$_2$CO$_3$ (3.3 equiv.)–MeI (20 equiv.) in boiling acetone for 20 h. The trimethoxy derivative [^{1}H NMR (CDCl$_3$): 0.58 (s, 27 H), 0.66 (s, 27 H), 1.18 (s, 18 H), 1.27 (s, 18 H), 1.52 (s, 6 H), 1.63 (s, 6 H), 3.46 (s, 9 H, OMe), 3.86 (s, 12 H, ArCH$_2$), 6.78 (s, 3 H, OH), 6.93 (s, 6 H, H$_{Ar}$), 6.97 (s, 6 H, H$_{Ar}$)] was separated over silica gel 60 with CH$_2$Cl$_2$ (R_f = 0.35, yield 15% after workup) from the tetramethoxy by-product, treated with ethyl bromoacetate (13.5 equiv.)–NaH (9 equiv.) in hot THF for 12 h to substitute OH by OCH$_2$CO$_2$OEt in **2b** [MS (EI): 1568; ^{1}H NMR (CDCl$_3$): 0.63 (s, 36 H), 0.73 (s, 9 H), 0.87 (s, 27 H), 1.34 (t, 9 H, Me ester), 1.43 (s, 24 H), 1.85 (s, 6 H, CH$_2$), 2.34 (s, 9 H, OMe), 3.46 (d, 6 H, ArCH$_2$), 4.30 (m, 6 H, C*H*Me), 4.53 (d, 6 H, ArCH$_2$), 4.69 (s, OCH$_2$), 6.64 (s, 6 H, H$_{Ar}$), 7.24 (s, 6 H, H$_{Ar}$); conformation: *cone*.] This was then finally hydrolysed with NMe$_4$OH in boiling THF to give **2** [^{13}C NMR (CD$_3$OD; 295 K): 172.03, 155.15, 151.76, 146.09, 145.75, 133.88, 129.27, 125.73, 69.87, 61.04, 57.32, 57.1, 38.61, 38.53, 32.91, 32.67, 32.55, 32.16, 31.06, 30.57; ^{1}H NMR: 0.66, 0.86, 1.39, 1.41, 1.5, 1.84, 2.62 (br s), 3.5–4.5 (br), 4.5 (br s), 6.75, 7.24].

¶ *Synthesis* of **3**: *p-tert*-Butylcalix[6]arenehexaol was treated with Cs$_2$CO$_3$ (3 equiv.)–MeI (8 equiv.) in boiling acetone for 8 h. The product mixture was reacted with ethyl bromoacetate–NaH, recrystallized and separated by prep. HPLC [71Si4A, CH$_2$Cl$_2$–EtOAc (5%)–MeOH (0.5%)], to give the trimethoxy tris(ethoxycarbonyl)methoxy precursor **3a** [44.7% yield; MS (EI): 1273; TLC (CH$_2$Cl$_2$–ethyl acetate 95 : 5, silica gel 60): R_f = 0.93; ^{1}H NMR (CDCl$_3$): 0.96(s) and 1.07 (s + m) (27 H), 1.25–1.33 (m, 24 H), 1.39 (s, 12 H), 2.1 (br s, 3 H), 2.83 (s, 2 H), 3.44 (s, 2 H), 3.4–4.22 (br m, 22 H), 4.44 (br s, 4 H), 6.68 (s, 2 H), 6.91–7.01 (m, 6 H), 7.2 (d, 4 H)]. **3a** was then hydrolysed by NMe$_4$OH in boiling THF to **3** [^{1}H NMR (CDCl$_3$–CD$_3$OD 1 : 1): 1.12 (s, 45 H), 1.2 (s, 9 H), 3.52 (br s, 15 H, Ar-CH$_2$ and OMe), 4.0 (br s) and 4.5 (br m) (10 H, ArCH$_2$ and OCH$_2$), 6.91 (s, 2 H), 6.96 (s, 4 H), 7.02 (s, 4 H), 7.08 (s, 2 H), 8.5 (s, 3 H, OH)].

|| *Synthesis* of **4**: Removal of the protective methyl groups in the NaClO$_4$ complex of precursor **2b** with Me$_3$SiI (6.7 equiv.) in boiling CHCl$_3$ for 20 h gives intermediate **4b** after workup [TLC, (CHCl$_3$–MeOH 5 : 1): R_f = 0.91; MS (EI): 1568 (no higher masses); ^{1}H and ^{13}C NMR (CDCl$_3$): disappeared 2.34 and 60.4 (OMe), H$_{Ar}$: 6.99–7.10 (4 s)]. Treatment of **4b** with *N*,*N*-diethylchloroacetamide–NaI–K$_2$CO$_3$ (12 equiv. each) in boiling acetone for 20 h yields **4c** [72% yield after workup; MS (EI): 1907; TLC (CHCl$_3$–MeOH 5 : 1): R_f = 0.87; ^{13}C NMR (CDCl$_3$): new 41.2, 40.2, 12.9 [N(C$_2$H$_5$)$_2$]. Selective hydrolysis of the ester groups with NMe$_4$OH in boiling THF then gives **4** [^{13}C NMR (CDCl$_3$): 170.8, 167.94, 153.28, 151.88, 145.88, 145.31, 132.9, 131.9, 129.19, 124.16, 71.97, 69.74, 56.59, 41.59, 40.16, 37.99, 37.82, 37.73, 32.25–30.0, 13.98, 12.43; proposed conformation: *cone*; TLC (CHCl$_3$–MeOH 5 : 1): R_f = 0.44].

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