

Selective extraction of naturally occurring radioactive Ra²⁺

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Organic extractants play a significant role in the selective removal of radioactive cations from waste streams. Although, literature on the selective removal of man-made radioactive material such as Americium (Am) is widespread, the selective removal of naturally occurring radioactive material such as Ra²⁺ is only mentioned sporadically. This *tutorial review* deals with the selective extraction of the highly radiotoxic Ra²⁺. Special attention is paid to different types of organic extractants used.

Introduction

Ra²⁺ is found as a daughter nuclide of both the Naturally Occurring Radioactive Materials (NORM)¹ uranium (U) and thorium (Th), which in turn are associated with many different minerals and rock types. Highly mineralised formation waters or brines, leach Ra²⁺ from the rocks, thus obtaining a “high” NORM content.² Consequently, Ra²⁺ is a subsurface pollutant in *e.g.* ores, oil and gas, and in drinking water.

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One of the main industries with an aqueous “Technologically Enhanced NORM” TENORM problem, is the petroleum industry. The sedimentary rocks, shales, within which oil and gas deposits are found, contain Ra²⁺ holding formation water. This formation water is transported to the surface together with *e.g.* sulfate-rich injected (sea) water.³ When the produced water is brought to the surface it contains traces of Ra²⁺, together with an abundance of other cations, mainly alkali(ne earth) (Table 1), and organic compounds.³

Due to the global distribution of Ra²⁺, it can be both ingested with food and inhaled. Subsequently,⁵ it follows similar accumulation pathways as Ca²⁺ and contributes considerably to the internal dose of radioactivity.



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March 2005, he obtained his PhD from the Supramolecular Chemistry and Technology group of Prof. Dr. Ir. D. N. Reinhoudt at the University of Twente, the Netherlands. His thesis was entitled “Selective extraction of naturally occurring radioactive Ra²⁺ from aqueous waste streams”. From July 2005 he is a postdoctoral researcher in the Chemical Biology group of Dr. H. Ovaa at The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, The Netherlands. His research will focus on the biomolecular imaging of enzymatic activities *in vivo*, using both fluorescence-based and (radio)labeled molecular probes.

Willem Verboom was born in 1954 in Goes, The Netherlands. He studied chemistry at Utrecht University, where he also received



Willem Verboom

his PhD with Prof. Dr. H. J. T. Bos with a thesis entitled “Thermal and photochemical rearrangements of γ -oxo- α,β -unsaturated carboxamides and esters”. Subsequently, he joined the group of Prof. Dr. Ir. D.N. Reinhoudt at the University of Twente, where he now is an associate professor in organic chemistry. Over the years the research interests moved from heterocyclic chemistry to supramolecular chemistry. His present research topics involve the functionalization and application of suitable molecular building blocks, in particular calixarenes and cavitands, for the development of specific receptors and larger (non-)covalent assemblies and recently, chemistry in microchips. He is the (co-)author of about 280 scientific publications. He served as a board member of the International Society of Heterocyclic Chemistry in the period 1992–1995. He was a member of the editorial board of the Dutch journal “Recl. Trav. Chim. Pays-Bas (1992–1996)”. For many years now he has refereed papers for journals of the Royal Society of Chemistry. Currently, he is secretary of the ‘Design and Synthesis’ study group of the Council for Chemical Sciences of the Netherlands Organization for Scientific Research (CW-NWO) (2001–)

Table 1 Alkali(ne earth) cation contents of formation, sea, and production water (400 g L⁻¹ of dissolved solids)³

Ion	Formation water (M)	Sea water (M)	Produced water (M) ⁴
Na ⁺	1.3	4.8×10^{-1}	1.5
K ⁺	1.7×10^{-2}	1.2×10^{-2}	Not reported
Mg ²⁺	1.6×10^{-2}	5.7×10^{-2}	3.7×10^{-2}
Ca ²⁺	1.2×10^{-1}	1.1×10^{-2}	8.2×10^{-2}
Sr ²⁺	8.7×10^{-3}	0	1.5×10^{-3}
Ba ²⁺	2.0×10^{-3}	0	6.9×10^{-4}

Furthermore, the Ra²⁺ gaseous daughter nuclide radon (Rn) is retained in the lungs, where it decays to Pb and Po. This highly toxic nature of Ra²⁺ renders effective separation of these toxic radionuclides from other non-toxic substances highly desirable.

Mme. Curie was the first to isolate Ra²⁺ by way of fractional precipitation of the RaCl₂ salt.⁶ Currently, a typical pre-precipitation technique for Ra²⁺ involves an initial co-precipitation of Ra²⁺ with Ba²⁺ or Pb²⁺ sulfates, carbonates, or chromates.⁷ Elution from (ion exchange) columns, using *e.g.* ammonium citrate, is another common way to isolate Ra²⁺.⁸ A technique, often used to analyze the Ra²⁺ content of water-streams, is the non-specific binding of alkaline earth cations on magnesium oxide surfaces⁹ or hydrous titanium oxide.¹⁰ The chemical properties of Ra²⁺ cations can also be used to immobilize them in synthetic clay. Na-4-mica (Na₄Al₄Si₄Mg₆O₂₀F₄·xH₂O) has a high Ra²⁺ selectivity,¹¹ its high charge density and special layer stacking allows for the

uptake of the less hydrated cations such as Ra²⁺. This mica can be used both to separate Ra²⁺ from Na⁺ and as fixation for safe disposal. Drinking water production units use Ra²⁺ separation technologies not specifically designed for its removal such as ion exchange, reverse osmosis, lime softening, green sand filtration, co-precipitation with barium sulfate, hydrous manganese oxide filtration, electro dialysis reversal, activated alumina, and enhanced coagulation/filtration.¹²

The techniques mentioned above can be used to remove Ra²⁺ cations from aqueous solutes, but they are not selective. An alternative approach to remove Ra²⁺ from aqueous streams is solvent extraction using a Ra²⁺ specific extractant. For the design of Ra²⁺ selective extractants there must be a difference in complexation properties compared to the alkali(ne earth) cations Na⁺, K⁺, Mg²⁺, Ca²⁺, Sr²⁺, and Ba²⁺ of which a significant excess is present (see Table 1). Since of all the alkaline earth elements, Ra²⁺ has the lowest tendency to form complexes,¹³ this challenge is substantial.

In this review the different approaches to complex Ra²⁺ using organic extractants are described. A direct comparison between the results of different studies is not often possible, since the reported results have been obtained with different extraction techniques and under different conditions.

Resin-based ²²⁶Ra²⁺ extraction

For Ra²⁺ extraction there are two known methods, *viz.* a neutral extractant immobilized on a solid support, or a neutral extractant, which forms a complex with a negatively charged support.

The complexation behavior of alkaline earth cations by neutral extractants (Chart 1) depends on matching of the size of cation and extractant. The extractant should be large enough to incorporate Ra²⁺ cations (1.48–1.70 Å), and it should possess oxygen donor atoms, because Ra²⁺ is a hard Lewis-acid.¹³



David N. Reinhoudt

Professor David N. Reinhoudt was born in 1942 in The Netherlands. He studied Chemical Technology at the Delft University of Technology and graduated (summa cum laude) in chemistry in 1969 with Professor H. C. Beijerman. In the period 1970–1975 he worked at Shell where he started the crown ether research program. In 1975 he was appointed as a part-time professor (extra-ordinarius) at the University of Twente followed by appointment as a full professor in

*1978. The major part of his research deals with supramolecular chemistry and technology. (Nanotechnology, molecular recognition, and non-covalent combinatorial synthesis are the major fields. Application of supramolecular chemistry *e.g.* in “lab-on-a-chip”, in the field of electronic or optical sensor systems, catalysis, and molecular materials.) Professor Reinhoudt is the scientific director of the MESA⁺ Research Institute. Since 2002 he has been the chairman of the Board of NanoNed, the Dutch Network for Nanotechnology. He is a member of the Royal Dutch Academy of Sciences, Fellow of the American Association for the Advancement of Science, and Fellow of the Institute of Physics. He is the author of more than 800 scientific publications, patents, review articles, and books. He has been honored with the Izatt-Christensen award (1995), the Simon Stevin Mastership (1998) and Knight of the Order of the Dutch Lion (2002).*

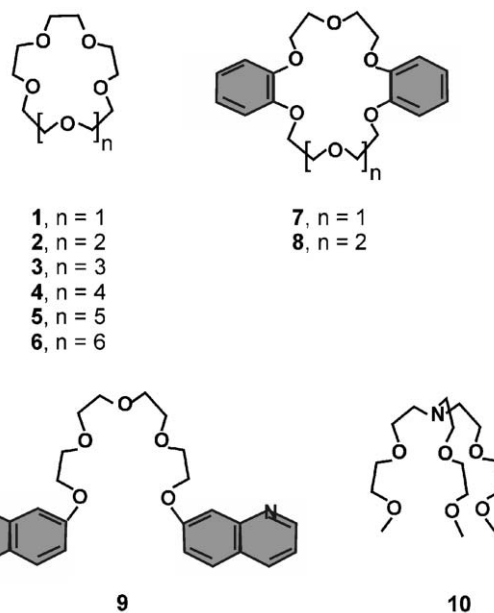


Chart 1 Neutral crown ether derivatives.

Benzi *et al.*¹⁴ reported Ra^{2+} extraction by several podands and crown ethers on either Amberlite XAD resins or Kieselgel. 1,11-Bis(8-quinolyloxy)-6,9-trioxundecane (Kryptofix 5 (**9**)) and tris(2-methoxyethoxyethyl)amine (**10**) exhibit a high Ra^{2+} extraction under non-competitive conditions, whereas 18-crown-6 (**2**), dibenzo-18-crown-6 (**7**), and 24-crown-8 (**4**) are less effective. The amount of free extractant or Ra^{2+} complex in the aqueous solution has not been determined, although this could have a significant influence on the extraction percentages.

The 3M company has immobilized crown ethers (type not specified) *via* covalent attachment to a silica surface, to extract various cations, such as Ra^{2+} from aqueous solutions (3M Empore[®]).¹⁵

Cation exchangers are negatively charged and as such can nonselectively bind cations, including Ra^{2+} . Dietz *et al.*¹⁶ showed that the addition of water-soluble crown ethers (**1–6**) gives rise to a cooperative (synergistic) effect, inducing selectivity by forming [(solid support)^{*n*-}· Ra^{2+} ·(crown-ether)]^{*n*-2} complexes. A cation exchanger in combination with a significant excess of a crown ether, resulted for 18-crown-6 (**2**) in higher formation constants (log *K* values) for Ra^{2+} (3.7) and Ba^{2+} (3.9), compared to Ca^{2+} (1.1) and Sr^{2+} (3.0).¹⁶ The most efficient cation exchanger for the synergistic extraction of Ra^{2+} cations was Bio-Rad AG MP-50.

Anionic polydentate extractants

Since Ra^{2+} cations are divalent the charge has to be compensated to form (neutral) complexes. Consequently, a common Ra^{2+} extraction technique is based on the use of electrostatic forces, applying amino carboxylic, alkyl phosphoric, sulfonic, and alkyl carboxylic acids.¹³

For example, Sekine *et al.*¹⁷ reported that (water-soluble) amino carboxylic acids **12–16** have stability constants for Ra^{2+} with log $K_{\text{ex}} \geq 5.6$ (M^{-1}). Of these extractants diethylenetriamine-*N,N,N',N'',N'''*-pentaacetic acid (**13**) and *trans*-1,2-diaminocyclohexane-*N,N,N',N''*-tetraacetic acid (**15**) exhibit the highest log K_{ex} values of 8.5 and 8.3, respectively. For extractants **12–16**, the K_{ex} values are high enough to obtain efficient extraction for Ra^{2+} cations from an organic phase containing the non-selective extractants 2-thenoyltrifluoroacetone (**11**) and tributylphosphate (**17**). In general the extraction constants of Ra^{2+} are lower than those of the other alkaline earth cations.¹⁷ This indicates that amino carboxylic acids cannot function as selective Ra^{2+} extractants in waste streams containing competing alkaline earth cations.

Alternatives to amino carboxylic acids are phosphoric acids. Nitrilobis(methylene)triphosphonic acid (**21**) has a stability constant for Ba^{2+} of log K_{ex} 6.5 and has a similar value for

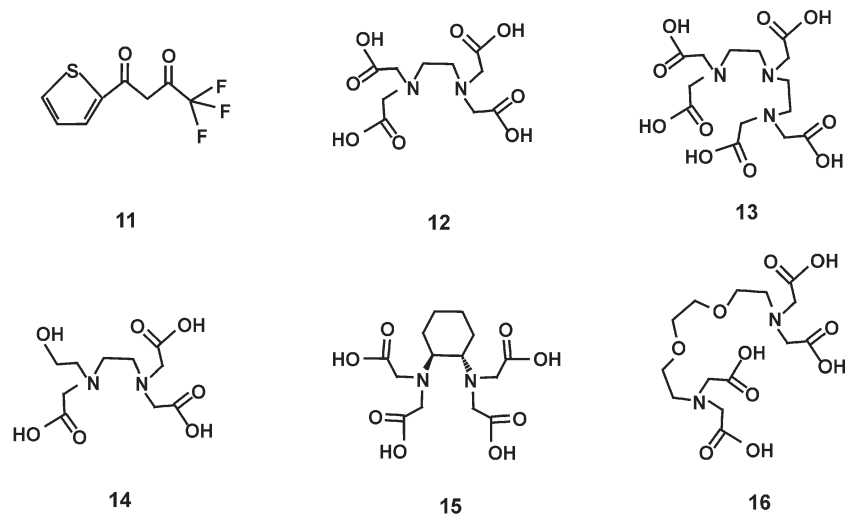


Chart 2 2-Thenoyltrifluoroacetone (**11**) and polydentate amino carboxylic acids (**12–16**) as Ra^{2+} extractants.

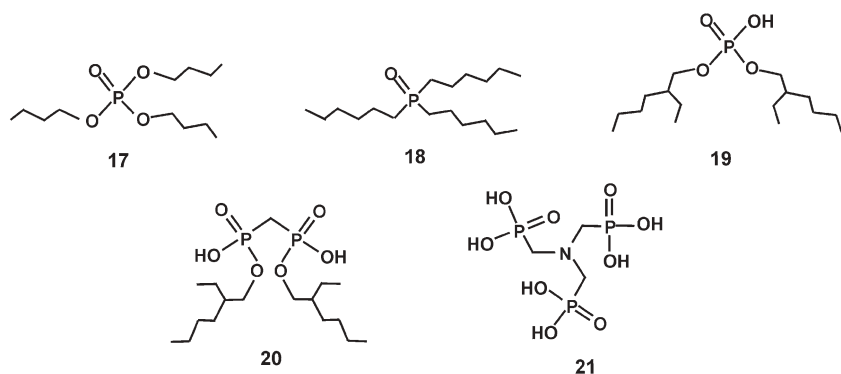


Chart 3 Phosphorus-based extractants.

Ra²⁺.¹⁸ Bis(2-ethylhexyl)phosphoric acid (**19**) extracts Ra²⁺ at highly acidic conditions from a mixture of ²²⁷Ac, ²²³Ra, ²²⁷Th, and ²³³Fr.¹⁹ However, a similar extracting agent, *P,P'*-bis(2-ethylhexyl)ethanediphosphonic acid (**20**), is hardly selective for the alkaline earth cations.²⁰ In general, the alkaline earth cation selectivity of phosphoric acids is assumed to be in the order Ca²⁺ >> Sr²⁺ > Ba²⁺ > Ra²⁺.²¹

Although they are not Ra²⁺ selective in the alkaline earth series, both amino carboxylic acids and phosphoric acids are often used when no real selectivity is desired *e.g.* for the non-selective removal of Ra²⁺ from ion exchange resins.²²

Hendriksen *et al.*²³ described the use of *p*-*tert*-butylcalix[4]-arene tetracarboxylic acid (**24**) as carboxylic acid-based Ra²⁺ extractant. The relative extraction constants of tetracarboxylic acid (**24**) have been obtained by back-extraction experiments using another water-soluble extractant, DTPA (**13**), 1,4,7,10-tetraazacyclododecan-1,4,7,10-tetraacetic acid (DOTA (**22**)), or 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (Kryptofix 2.2.2 (**23**)).²³ The relative extraction constants of **24** (K_{24}) are: $5.7 \times K_{13}$, $2.2 \times K_{22}$, and $3.5 \times K_{23}$. The difference between the K -values of DTPA (**13**) and DOTA (**22**) might be due to both the difference in the number of carboxylic acid substituents or to the macrocyclic effect claimed for DOTA (**22**). A similar experiment with EDTA (**12**), rather than DTPA (**13**), would clarify which factor is the most decisive. These data suggest that in aqueous media, a neutral strapped macrocyclic cage (Kryptofix 2.2.2 (**23**)) is almost as important for effective Ra²⁺ complexation as the presence of four carboxylic acid groups on a macrocycle (DOTA (**22**)).

Unfortunately, extraction results for alkaline earth cations other than Ra²⁺ have not been reported, making it hard to conclude whether calix[4]arene tetracarboxylic acid (**24**) is Ra²⁺ selective. However, the kinetic stability of a Ra²⁺ complex with 2 mM tetracarboxylic acid (**24**) in the presence of a mixture of Na⁺ (150 mM), K⁺ (2.5 mM), Mg²⁺ (2.5 mM), Ca²⁺ (2.5 mM), and Zn²⁺ (2.5 mM) has been studied.²³ Under these conditions 62% of the ²²³Ra²⁺ cations remained in the organic phase, proving the high Ra²⁺ complex stability of this particular extractant.

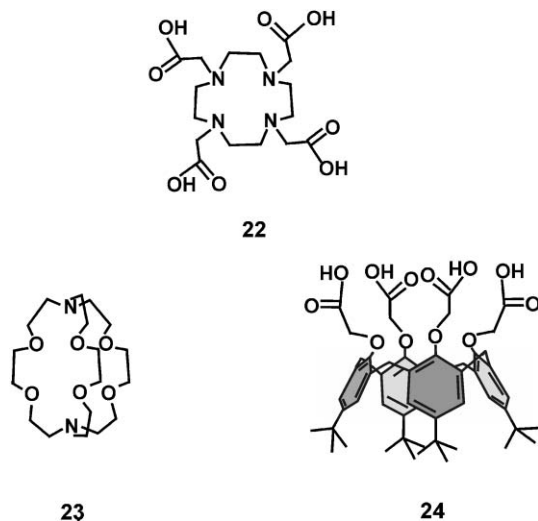


Chart 4 Ra²⁺ extractants evaluated by Hendriksen *et al.*²³

To determine the effect of the number of carboxylic acid groups on a platform on the ²²⁶Ra²⁺ selectivity, in our group we have studied thiacalix[4]arene carboxylic acids (Chart 5) for their Ra²⁺ selectivity in the presence of an excess of Ca²⁺, Sr²⁺, or Ba²⁺ (Table 2).²⁴

The data in Table 2 show that a thiacalix[4]arene with two carboxylic acid groups (**25**) has the highest Ra²⁺ selectivity in the presence of Ca²⁺ and Sr²⁺. Furthermore, it can be concluded that increasing the number of carboxylic acid groups gives an overall decrease in Ra²⁺ selectivity.

Synergistic Ra²⁺ extractants

Since the dehydration and transfer of anions into organic solvents is difficult, neutral extractants are not very effective for the extraction of Ra²⁺ into organic solvents.²⁵ A way to improve both the extraction efficiency and selectivity, is to make use of the cooperation (synergism) between two systems by using an electrostatic agent to drive the extraction in combination with a selective neutral complexing agent.²⁵

For example, the combination of 2-thenoyltrifluoroacetone (**11**) and tributylphosphate (**17**) or trioctylphosphine oxide (**18**) was used by Šebesta and Havlik to extract Ra²⁺ cations, resulting in (Ra(**11**)₂(L)_s)_{org} complexes (L = **17** or **18**),²⁶ while **17** and **18** alone do not give Ra²⁺ extraction.

Despite these results, the majority of the research on Ra²⁺ selective extractants is based on “size-selective synergism”.²⁵ This approach generally utilizes the macrocyclic cage of a crown ether for size selectivity, and complementary acidic groups for the neutralization of the divalent cations.²⁵

Mc Dowel *et al.*²⁷ reported that a 2:1 mixture of dicyclohexano-21-crown-7 (dc-21-crown-7 (**28**)) and 2-hexyl-2-methyldecanoic acid (**29**) gave a Ra²⁺ distribution coefficient ($D_{Ra} = Ra_{org}/Ra_{aq}$) larger than 200. In addition, this combination of extractants has high separation factors (D_{Ra}/D_M) for the other alkaline earth cations (Table 3).

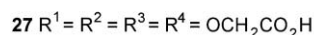
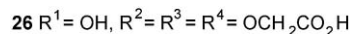
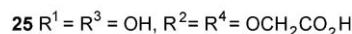
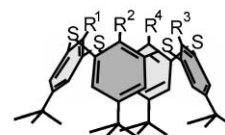


Chart 5 Carboxylic acid-containing thiacalix[4]arenes.

Table 2 Selectivity coefficients ($\log(K_{ex}^{Ra}/K_{ex}^M)$)^a of ionophores **25–27**²⁴

Compd	$\log(K_{ex}^{Ra}/K_{ex}^{Ca})$	$\log(K_{ex}^{Ra}/K_{ex}^{Sr})$	$\log(K_{ex}^{Ra}/K_{ex}^{Ba})$
25	1.2	1.5	−0.36
26	−1.2	0.22	−0.18
27	<−0.56 ^b	<−1.2 ^b	<−0.45 ^b

^a Extraction constants are corrected for the binding stoichiometries of the different extractants used. ^b Due to the low ²²⁶Ra²⁺ extraction percentages obtained, these values indicate upper limits.

Table 3 Separation factors (D_{Ra}/D_M) obtained with various crown-ether acid combinations^{27,28}

Cation	Separation factor (D_{Ra}/D_M)			
	28 + 29^a	1 + 30^b	2 + 30^b	3 + 30^b
Ba ²⁺	9.3	1.2	1.9	2.7
Sr ²⁺	12.3	6.2	2.8	5.5
Ca ²⁺	58	41	140	350
Mg ²⁺	560	—	—	—

^a The aqueous phase contained 5.0×10^{-8} M Ra²⁺, 4 M Na⁺, and 0.01 M M(NO₃)₂ (M²⁺ = Be²⁺, Ca²⁺, Sr²⁺, or Ba²⁺), while the organic phase contained 0.10 M **28** and 0.05 M **29**.²⁷ ^b The aqueous phase contained tracers of ⁴⁵Ca²⁺, ⁸⁵Sr²⁺, ¹³³Ba²⁺, and ²²³Ra²⁺ (very low concentrations expected), while the organic phase contained 0.01 M **30** and 0.001 M crown ether (1–3).²⁸

However, it should be noted that these separation factors are measured in the presence of a fifty-fold excess of dc-21-crown-7 (**28**) compared to the concentrations of competing cations. Ra²⁺ extraction starts to decrease significantly at M(NO₃)₂ concentrations between 10⁻² and 10⁻¹ M. Nevertheless, Ra²⁺ extraction in the presence of large excesses of Na⁺ is still effective.²⁷

Ra²⁺ separation was also achieved by Dietz *et al.*¹⁶ using water-soluble crown ethers in solvent extraction studies similar to the experiments performed with cation exchange resins (see above). In this case an organic solution of dinonylnaphthalenesulfonic acid (**30**) was used as neutralizing agent. The Ra²⁺ selectivity of 15-crown-5 (**1**), 18-crown-6 (**2**), and 21-crown-7 (**3**) has been determined in the presence of the other alkaline earth cations (Table 3).²⁸ Since dinonylnaphthalenesulfonic acid (**30**) alone showed very little selectivity along the series of the alkaline earth cations, the obtained Ra²⁺ selectivities have been attributed to the crown ethers. For Ca²⁺ and Ra²⁺ separation factors (D_{Ra}/D_{Ca}) above 40 have been found, while D_{Ra}/D_{Sr} and D_{Ra}/D_{Ba} were rather small (Table 3). Increasing the crown ether size from 15-crown-5 (**1**) to 21-crown-7 (**3**) improves the Ra²⁺ separation factors in the presence of Ca²⁺, Sr²⁺, and Ba²⁺.²⁹ Furthermore, Chiarizia *et al.*²⁹ showed that an excess of tributylphosphate (**17**) in the organic phase, compared to dinonylnaphthalenesulfonic acid (**30**), decreased the Ra²⁺ extraction, suggesting that tributylphosphate (**17**) interferes with the synergism of the crown ether and dinonylnaphthalenesulfonic acid (**30**).

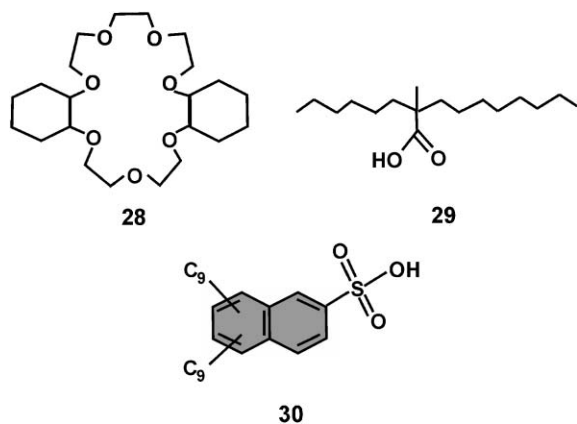


Chart 6 Crown ether-based synergistic extractant combinations.

Rajec *et al.*³⁰ used a combination of 18-crown-6 (**2**) and tungstosilicic acid (H₄SiW₁₂O₄₀·30H₂O) to co-precipitate Ra²⁺ with Sr²⁺ or Ca²⁺ cations. Compared to the stability constants of Ca²⁺ (18.2) and Sr²⁺ (776.2), that of ²²³Ra²⁺ has been estimated to be 2366.

To provide insight into the Ra²⁺ selectivity of synergistic systems in the presence of an excess of the competing cations Ca²⁺, Sr²⁺, or Ba²⁺, in our group we have studied two synergistic approaches.²⁴ The first uses a thiacalix[4]crown-6 (**31**), a crown-ether derivative which is selective for Cs⁺,³¹ a cation with a similar size as Ra²⁺,¹³ in combination with two equivalents of pentadecanoic acid (**32**). The second method involves thiacalix[4]arene dicarboxylic acid (**25**) in combination with db-21-crown-7 (**8**), the conventional crown ether (size) that induces the highest Ra²⁺/(alkaline earth cation) selectivity (see above).

Fig. 1 clearly shows that the combination of the thiacalix[4]crown-6 (**31**) with pentadecanoic acid (**32**) does not provide Ra²⁺ extraction at Ca²⁺, Sr²⁺, or Ba²⁺ concentrations exceeding that of the extractant used. On the other hand, the Ra²⁺ selective thiacalix[4]arene dicarboxylic acid (**25**) shows a significantly improved Ra²⁺/Ca²⁺ selectivity in a synergistic mixture with db-21-crown-7 (**8**). However, the Ra²⁺/Sr²⁺ and the Ra²⁺/Ba²⁺ selectivities do not change in the presence of the crown ether.

Combination of acid groups and crown ethers on a platform

In order to optimize the combination of electrostatic and macrocyclic effects, a logical step is the use of crown ethers functionalized with pendant acid groups. This system was first introduced by Strzelbicki and Bartsch³² and gives an increased extraction of alkali(ne earth) cations compared to the crown ether alone.

The non-competitive Ra²⁺ extraction behavior of eleven different crown-ether monocarboxylic acid derivatives (Chart 8; top) has been evaluated by Beklemishev *et al.*³³ Unfortunately, no direct comparison between the combination of a crown ether–acid combination and a separate crown ether or acid has been made. First of all the crown ether cavity size has been evaluated, showing that dibenzo-22-crown-7 monocarboxylic acid (**36**; R¹ = R² = R³ = H) gave the highest distribution coefficient for Ra²⁺ ($D_{Ra} = 0.5$). Only the second smallest crown ether, dibenzo-16-crown-5 monocarboxylic

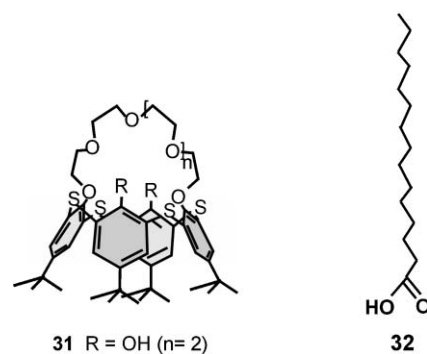
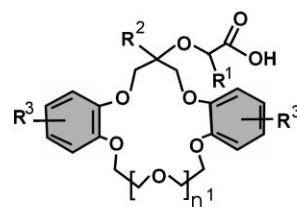


Chart 7 Thiacalix[4]crown-based synergistic extractant combination.

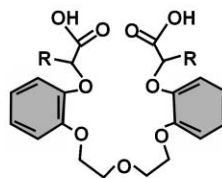
acid (db-16-crown-5-ma (**33**)), has been further optimized by increasing the lipophilicity; with $R^1 = n$ -decyl ($R^2 = R^3 = H$) D_{Ra} is 2.0, with $R^2 = n$ -hexadecyl ($R^1 = R^3 = H$) D_{Ra} is 2.8, and with $R^3 = tert$ -butyl ($R^1 = R^2 = H$) D_{Ra} is 23. These results reveal the positive influence of an increased lipophilicity of the crown ethers on the Ra^{2+} extraction. In an extension of this study Chu and Lin³⁴ reported the selectivity of db-16-crown-5-ma (**33**) ($R^1 = R^2 = H$ and $R^3 = tert$ -butyl) towards the alkaline earth cations. The reason for using db-16-crown-5-ma (**33**), instead of *e.g.* db-22-crown-7-ma (**35**), is the lower price, rather than an optimized macrocyclic effect. With an excess of extractant (10^{-3} M) a significant competition in the Ra^{2+} extraction was observed when the concentrations of the competing alkaline earth cations were 10^4 times higher than that of $^{226}Ra^{2+}$ ($56 \text{ Bq ml}^{-1} = \sim 10^{-9} \text{ M}$). Chen *et al.*³⁵ reported that in competition experiments, the Ra^{2+} extraction percentage remains below 20% in all cases. However, no competition has been observed for similar K^+ concentrations, a result that has been attributed to the different valency and chemical properties of K^+ cations.³⁴

Another possibility to combine a crown ether derivative with acidic groups is the attachment of two acidic substituents to a calix[4]crown. The two phenol groups of a calix[4]crown allow for two acid groups to be positioned adjacent to the crown-ether bridge, resulting in both complete neutralization and size selective complexation of alkaline earth cations. Chen *et al.*³⁵ reported the Ra^{2+} selectivity in the presence of alkaline earth cations, using two different acid-functionalized extractants (Chart 8). Under the conditions used, the calix[4]crown diacids **38** and **39** showed the highest Ba^{2+} and Ra^{2+} selectivities compared to db-16-crown-5-ma (**33**; $R^1 = R^2 = H$ and $R^3 = tert$ -butyl) and a podand containing two carboxylic acid groups (**37**). Where the calix[4]crown diacids **38** and **39** only showed high affinities for Ba^{2+} and Ra^{2+} cations, db-16-crown-5-ma (**33**) and the podand **37** do not give distinct differentiation between the different alkaline earth cations.

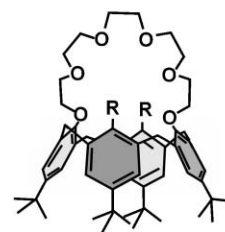
Back extractions with the water-soluble extracting agent EDTA (**12**) have been used to determine the relative extraction constants of the calix[4]crown diacids **38** and **39** in chloroform;



33; $n = 0$
34; $n = 1$
35; $n = 2$
36; $n = 3$
 $R^1 = H, \text{ phenyl}, n\text{-decyl}, n\text{-octadecyl}$
 $R^2 = H, n\text{-dodecyl}, n\text{-tetradecyl}, n\text{-hexadecyl}$
 $R^3 = H, t\text{-butyl}$



37; $R = n\text{-tetradecyl}$



38; $R = OCH_2CO_2H$,
39; $R = OCH_2C(O)NHOH$

Chart 8 Self-neutralizing extractants.

$K_{38} = 0.561 \times K_{12}$, while $K_{39} = 12.6 \times K_{12}$. In addition, pre-formed $^{223}Ra^{2+}$ complexes of both calix[4]crown-6 derivatives **38** and **39** showed a high kinetic stability. Less than 5% of the Ra^{2+} cations were removed after back extraction with aqueous phases containing Na^+ , K^+ , Mg^{2+} , Ca^{2+} , and Zn^{2+} (1 M; a tenfold excess of each cation to extractant).³⁵

To determine whether the Ra^{2+} extraction efficiency of calix[4]crown-6 dicarboxylic acid (**38**) could be fine-tuned by changing the crown-ether bridge cavity size, (thia)calix[4]-crown-5 and -6 dicarboxylic acids (**38**, **40**, **41**, and **42**; Charts 8 and 9) were studied for their Ra^{2+} selectivity.³⁶ Where Chen *et al.*³⁵ used an excess of extractant compared to a mixture of alkaline earth cations, we studied the Ra^{2+} selectivity with an

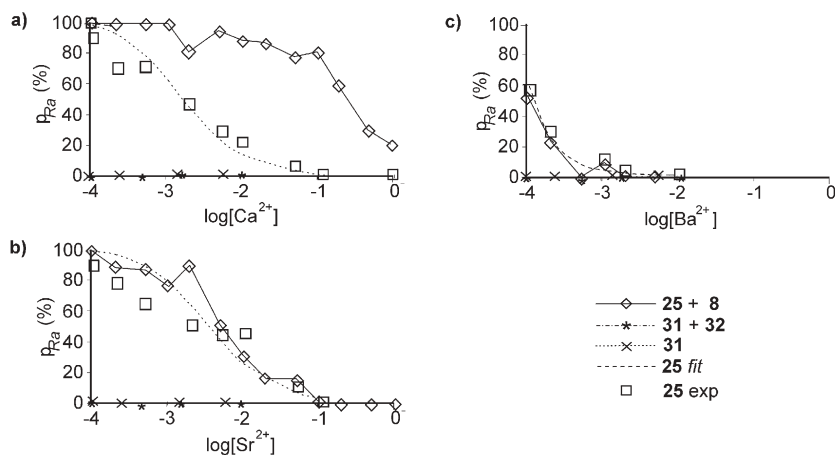
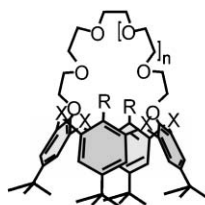


Fig. 1 $^{226}Ra^{2+}$ extraction percentages [$p_{Ra} = [^{226}Ra^{2+}]_{org}/[^{226}Ra^{2+}]_{tot}$ (%)] for different ratios of extractant [$L = 25, 25 + 8, 31$, and $31 + 32$] to $M(NO_3)_2$ [$M^{2+} = Ca^{2+}$ (a), Sr^{2+} (b), or Ba^{2+} (c)], and fixed extractant ($[25]_{tot} = [31]_{tot} = [8]_{tot} = 10^{-4} \text{ M}$ and $[32]_{tot} = 2 \times 10^{-4} \text{ M}$; 1 mL of CH_2Cl_2), and $[^{226}Ra^{2+}]_{tot}$ ($2.9 \times 10^{-8} \text{ M}$; pH 8.9 tris-HCl) concentrations.²⁴



- 40; X = CH₂, R = OCH₂CO₂H (n = 0)
 41; X = S, R = OCH₂CO₂H (n = 0)
 42; X = S, R = OCH₂CO₂H (n = 1)

Chart 9 Self-neutralizing (thia)calix[4]crowns.

excess of single competing alkali(ne earth) cations compared to extractant.

Based on the 1:1 stoichiometry of the alkaline earth complexes of the (thia)calix[4]crowns **38** and **40–42**,³⁶ the selectivity coefficients ($\log(K^{Ra}_{ex}/K^{M}_{ex})$) were determined (Table 4). From these data it is clear, that overall the crown-6 derivatives (**38** and **42**) give the highest Ra²⁺ selectivities, allowing for Ra²⁺ extraction from Mg²⁺/Ra²⁺, Ca²⁺/Ra²⁺, and Sr²⁺/Ra²⁺ ratios of 3.5×10^7 . When these two are compared, it can be concluded that in the presence of the alkaline earth cations most similar to Ra²⁺ (Sr²⁺ and Ba²⁺) the thiacalix[4]-arene platform induces a significant improvement in Ra²⁺ selectivity (K^{Ra}_{ex}/K^{M}_{ex}), viz. 212 and 52 times, respectively. Furthermore, thiacalix[4]crown-6 dicarboxylic acid (**42**) gives a higher extraction constant for Ra²⁺ than for Ba²⁺, where none of the other extractants have such a selectivity.

From the extraction curves a direct comparison of the Ra²⁺ selectivities can be made.³⁶ All four extractants show extremely high Ra²⁺/Rb⁺ and Ra²⁺/Cs⁺ selectivities, with more than 50% of the Ra²⁺ contents extracted at Rb⁺/Ra²⁺ and Cs⁺/Ra²⁺ ratios of 3.5×10^7 . A clear difference in Ra²⁺ selectivity can be observed in the presence of Na⁺ and K⁺ (Fig. 2). In the presence of Na⁺, thiacalix[4]crown-5 dicarboxylic acid (**41**) gives an extremely high Ra²⁺/Na⁺ selectivity, allowing for Ra²⁺ extraction ($\sim 70\%$) from a Na⁺/Ra²⁺ mixture with a ratio of 3.5×10^7 . On the other hand, with K⁺ both crown-6 derivatives **38** and **42**, give the highest Ra²⁺ selectivity. Since Na⁺ is the most abundant alkali cation in Ra²⁺ holding TENORM wastes (see Table 1),² this result indicates that thiacalix[4]crown-5 dicarboxylic acid (**41**) is the most efficient Ra²⁺ extractant in the presence of alkali cations.

To determine the influence of both the number and type of acid groups on the Ra²⁺ selectivity of thiacalix[4]crowns, the Ra²⁺ selectivity coefficients in the presence of Ca²⁺, Sr²⁺, or Ba²⁺ by thiacalix[4]crowns **43–46** were compared to those obtained with the thiacalix[4]crown dicarboxylic acids (**41** and **42**; Table 4).²⁴ The thiacalix[4]crown dicarboxylic acids (**41** and **42**) give the highest Ra²⁺ selectivity of the (thia)calix[4]crowns in the presence of Ca²⁺, Sr²⁺, or Ba²⁺. Consequently, two acid

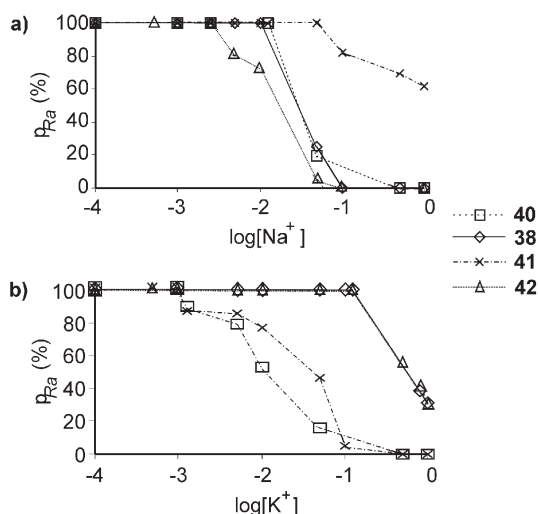


Fig. 2 ²²⁶Ra²⁺ extraction percentages [$p_{Ra} = [^{226}\text{Ra}^{2+}]_{\text{org}}/[^{226}\text{Ra}^{2+}]_{\text{tot}}$] (%) for different ratios of extractant (**38**, **40**, **41**, and **42**) to M(NO₃)₂ [M²⁺ = Na⁺ (a) and K⁺ (b)], and fixed extractant ([L] = 10⁻⁴ M; 1 mL of CH₂Cl₂), and [²²⁶Ra²⁺]_{tot} (2.9 × 10⁻⁸ M; pH 8.9 tris-HCl) concentrations.³⁶



- 43 R¹ = OH, R² = OCH₂CO₂H (n = 1) 46 R¹ = OH, R² = OCH₂CO₂H (n = 2)
 44 R¹ = R² = OCH₂CONHSO₂CH₃ (n = 1)
 45 R¹ = R² = OCH₂CONHSO₂CH₃ (n = 2)

Chart 10 Alternative self-neutralizing thiacalix[4]crowns.

substituents are most favorable for the Ra²⁺ selectivity of a thiacalix[4]crown and increasing the size of the acid substituents from carboxylic acid to bis(methylsulfonyl) carboxamides reduces the selectivity.

Self-assembled Ra²⁺ extractants

An alternative to the covalent Ra²⁺ extractants is the self-assembly of picrate (**47**) and guanosine (**48**), forming hexadecamers of **48** surrounded by four picrate (**47**) molecules, and the self-assembly of isoguanosine (**49**) forming decamers (Scheme 1).³⁷ Both guanosine-rich nucleic acids and synthetic (iso)guanosine derivatives are well known to coordinate alkali and alkaline earth cations using the G-quartet motif, work that has recently been highlighted in a review by Davis.³⁸ In our group we have studied these self-assembled systems for their

Table 4 ²²⁶Ra²⁺ selectivity coefficients ($\log(K^{Ra}_{ex}/K^{M}_{ex})$) for the extractants **38**, **40–42** in the presence of Mg²⁺, Ca²⁺, Sr²⁺, or Ba²⁺ cations³⁶

Extractant	$\log(K^{Ra}_{ex}/K^{Mg}_{ex})$	$\log(K^{Ra}_{ex}/K^{Ca}_{ex})$	$\log(K^{Ra}_{ex}/K^{Sr}_{ex})$	$\log(K^{Ra}_{ex}/K^{Ba}_{ex})$
40	3.7	1.1	0.3	-1.3
38	4.2	3.4	2.6	-0.5
41	4.2	3.5	1.7	-0.5
42	3.8	3.3	3.4	+0.9

Ra²⁺ selectivity in the presence of alkali(ne earth) cations, and under identical competitive conditions as mentioned above.³⁶

Fig. 3 shows a direct comparison of the extraction data with that obtained with the most selective covalent Ra²⁺ extractant thiacalix[4]crown-6 dicarboxylic acid (**42**).³⁶ The only difference in the Ra²⁺ selectivity determination is the range in which the extractants have been measured. Where thiacalix[4]crown-6 dicarboxylic acid was measured up to log (M²⁺) = 0,³⁶ the self-assembled extractants were measured up to log (M²⁺) = -1.6.³⁷ Nevertheless, except in the case of isoguanosine (**49**) and Mg²⁺, the difference in Ra²⁺ selectivity is apparent (Fig. 3).

Fig. 3d shows that in the case of Ba²⁺, the cation most similar to Ra²⁺, isoguanosine **49** equals the Ra²⁺/Ba²⁺ selectivity of the most Ra²⁺ selective covalent extractant, thiacalix[4]crown-6 dicarboxylic acid (**42**). However, in general the Ra²⁺ selectivities in the presence of competing alkaline earth cations of the noncovalent self-assembled systems (**47** + **48** and **49**) are lower

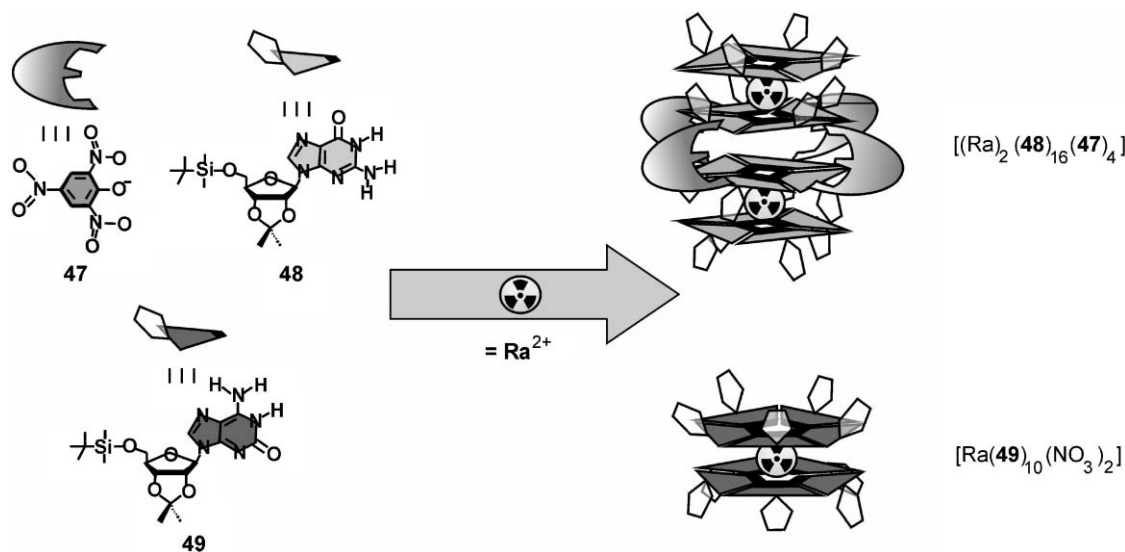
than that of **42**. Nevertheless, Ra²⁺ can still be efficiently extracted from M²⁺/Ra²⁺ (M²⁺ = Mg²⁺, Ca²⁺, or Sr²⁺) ratios of 10⁶ (Fig. 3a–c), which are remarkably high Ra²⁺ selectivities considering the simple molecules used.

When comparing the Ra²⁺ extraction behavior in the presence of alkali cations, isoguanosine (**49**) assemblies have the lowest Ra²⁺ selectivity of the two self-assembled systems.³⁷

In the alkaline earth cation series isoguanosine (**49**) provides the highest Ra²⁺ selectivity, while in the alkali cation series the picrate (**47**) guanosine (**48**) combination gives the highest Ra²⁺ selectivity. However, these selectivities do not exceed those of the optimised thiacalix[4]crown dicarboxylic acids (**41** and **42**).

Ra²⁺ extraction from real gas-field produced waters

Ra²⁺ has been extracted from gas-field produced water and a metal-ion based model solution using the thiacalix[4]crown



Scheme 1

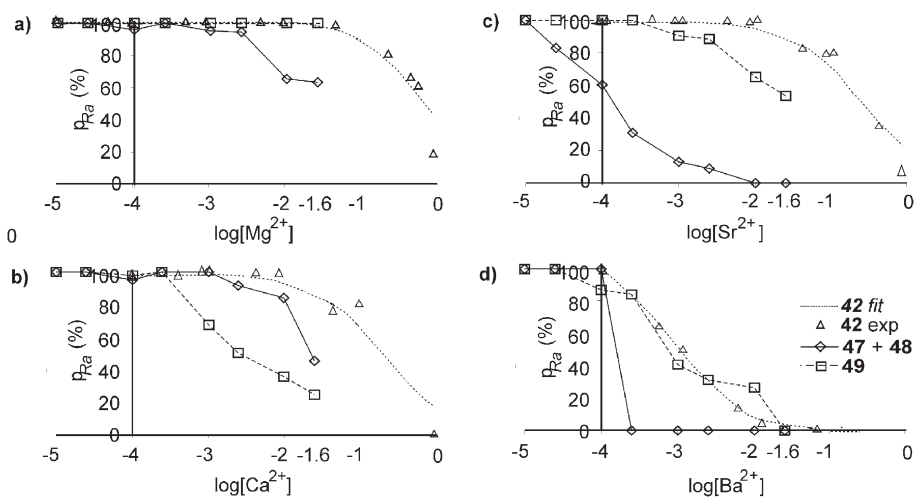


Fig. 3 ²²⁶Ra²⁺ extraction percentages [$P_{Ra} = [^{226}Ra^{2+}]_{org}/[^{226}Ra^{2+}]_{tot}$ (%)] for different ratios of extractant (**42**, **47** + **48**, and **49**) to $M(NO_3)_2$ [$M^{2+} = Mg^{2+}$ (a) and Ca^{2+} (b), Sr^{2+} (c), and Ba^{2+} (d)], and fixed extractant ($[48]_8 = [49]_{10} = [42] = 10^{-4}$ M; 1 mL of CH_2Cl_2), and $[^{226}Ra^{2+}]_{tot}$ (2.9×10^{-8} M; pH 8.9 tris-HCl) concentrations.³⁷

dicarboxylic acids (**41** and **42**) and (iso)guanosine (**48** and **49**).³⁹ Extraction of Ra²⁺ from the mixed metal ion containing gas-field produced water is possible with a significant excess of [Mⁿ⁺]_{tot} (Mⁿ⁺ = Na, K, Mg, Ca, Sr, Ba, Fe, Mn, Zn, Pb, U, Tl, Te, Cd, Ag, Mo, Cu, Ni, Co, Ti, Be and Ra ions) to [extractant]. In real produced water the thiacalix[4]crown-5 dicarboxylic acid (**41**) gave by far the highest Ra²⁺ selectivity, while in a model solution containing only the metal ion contents, the combination of picrate (**47**) and guanosine (**48**) was most effective. The latter suggests that the effectiveness of the self-assembled system may be reduced by the organic contents in the original produced water sample.³⁹ Furthermore, the fact that both thiacalix[4]crown-5 dicarboxylic acid (**41**) and the combination of picrate (**47**) and guanosine (**48**) give the most efficient Ra²⁺ extraction from these solutions, suggests that the most common cation, Na⁺ (0.7 M), causes most competition in the Ra²⁺ extraction from these waters.

Conclusions and outlook

Over the years different types of Ra²⁺ extractants have been developed. Neutral extractants alone do not give effective Ra²⁺ extraction and of the anionic polydentate extractants, the one only containing two anionic moieties provides the highest Ra²⁺ selectivity. The addition of a crown-ether derivative, giving rise to a synergistic mixture, improves the Ra²⁺ selectivity of the anionic polydentate extractants significantly, resulting in effective Ra²⁺/Mg²⁺ and Ra²⁺/Ca²⁺ separations. However, the covalent connection of both a crown-ether derivative and (two) anionic groups, in the form of (carboxylic) acids, gives improved Ra²⁺ selectivities and allows for effective Ra²⁺/alkali(ne earth) cation separation. Especially the (thia)calix[4]-crown dicarboxylic acids are highly selective Ra²⁺ extractants in the presence of competing alkali(ne earth) cations. An alternative type of Ra²⁺ extractants comprises the non-covalent self-assembly of (iso)guanosine derivatives. Although the latter ones exhibit a lower Ra²⁺ selectivity than the (thia)calix[4]crown dicarboxylic acids, the ability to extract Ra²⁺ using “simple” Ra²⁺ extractants provides a “cheap” alternative to these extractants.

Overall, the extraction data suggest that the Ra²⁺ selectivities reached are high enough to make extractants which have a Ra selectivity in the presence of an excess of alkali(ne earth) cations e.g. **38–49** applicable in (industrial) Ra²⁺ holding waste streams, and as such prevent public exposure to Ra²⁺.

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