Use of Dipicolinate-Based Complexes for Producing Ion-Imprinted Polystyrene Resins for the Extraction of Yttrium-90 and Heavy Lanthanide Cations

Anne-Sophie Chauvin,[a] Jean-Claude G. Bünzli,[a] François Bochud,[b] Rosario Scopelliti,[a] and Pascal Froidevaux*[b]

Abstract: Highly selective separation of yttrium (and lanthanides) is of interest for the design of radiopharmaceuticals, and an efficient method based on the ion-imprinting concept is proposed here. The synthesis and structural, thermodynamic and photophysical characterization of complexes of trivalent yttrium and lanthanides with two new vinyl derivatives of dipicolinic acid, HL1 and L2, are described. The feasibility of using ion-imprinted resins for yttrium and lanthanide separation is demonstrated. The resins were obtained by copolymerization with styrene and divinylbenzene and subsequent acid treatment to remove the metal ion. High-resolution Eu luminescence experiments revealed that the geometry of the complexation sites is well preserved in the imprinted polymers. The ion-imprinted polymer based on HL1 proved to be particularly well adapted for yttrium extraction, having a sizeable capacity (8.9 ± 0.2 mg g⁻¹ resin) and a fast rate of extraction (t₁/₂ = 1.7 min). In addition, lighter and heavier lanthanide ions are separated. Finally, the resin displays high selectivity for yttrium and lanthanide cations against alkali and alkaline earth metals. For instance, in a typical experiment, 10 mg of yttrium was extracted from 5 g of milk ash sample by 2 g of the resin. The good separation properties displayed by the resin based on HL1 open interesting perspectives for the production of highly pure ⁹⁰Y and radiolanthanides for medical applications, and for trace analysis of these radiochemicals in food and in the environment.

Keywords: copolymerization · extraction · lanthanides · polymers · yttrium

Introduction

Extraction and separation of metal cations have always been challenging analytical problems. Among the methods used, solid-phase extraction (SPE) is one of the most popular and efficient techniques. It merges the easy handling of a chromatographic method with the efficiency of solvent extraction. Recently, the preparation of new materials for metal-cation extraction based on the ion-imprinting concept was described: a matrix is synthesized in the presence of an ionic template and chelating resins are then obtained by removal of the targeted cation.[1-3] The cavities thus obtained in the polymer exhibit high selectivity towards specific metal ions, high capacity and the ability to deal with high concentrations of metal ions. Molecularly imprinted polymers have been successfully used as mimics of antibodies in an immunoassay-like technique[6,7] and of the active site of natural enzymes[8-10] as well as in biorecognition.[11] Moreover, D’Souza et al. have shown that synthetic polymers can be imprinted with motifs of crystal surfaces so as to template the growth of specific crystal phases.[22] The preparation of styrene-based ion-imprinted resins initially involves formation of a vinyl monomer host in the presence of a bound guest acting as template. This vinyl monomer–template host–guest complex is then polymerized with a cross-linking agent, which provides spatially regulated sites in the polymer matrix. Numerous studies describing such methodologies were carried out in order to separate transition

[a] Dr. A.-S. Chauvin, Prof. Dr. J.-C. G. Bünzli, Dr. R. Scopelliti
Laboratory of Lanthane Supramolecular Chemistry
École polytechnique fédérale de Lausanne
BCH 1402, 1015 Lausanne (Switzerland)

[b] Prof. Dr. F. Bochud, Dr. P. Froidevaux
Institute of Applied Radiophysics
University of Lausanne, Grand Pré 1
1007 Lausanne (Switzerland)
Fax: (+41)21-623-3435
E-mail: Pascal.Froidevaux@chuv.ch

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metal cations, but few have dealt with lanthanides or actinides, and none specifically with the yttrium cation.[13–18] Highly selective separation of yttrium and lanthanides is of interest for the design of radio-pharmaceuticals for the treatment of illnesses such as cancer and rheumatism, and in the past decades there has been significant interest in yttrium detection in biological applications.[19,20] Presently, $^{89}$Sr, $^{186}$Re, $^{153}$Sm, $^{166}$Ho, $^{168}$Er, $^{177}$Lu and $^{90}$Y radioisotopes are routinely used in clinical treatments,[21–23] and several $^{90}$Y-labelled biomolecules have been tested for their therapeutic efficacy in tumour radiotherapy.[24] Moreover, $^{90}$Sr, $^{90}$Y, radionlanthanides and actinides are gaining growing interest in radio-ecological analyses and are taken into account when assessing public exposure to ionizing radiation. Specific needs for analytical procedures for these radioelements led to the development of classical exchange and extraction resins.[25–28] However, all these techniques suffer either from low specificity, as in cation- or anion-exchange chromatography, or, in the case of the Eichrom Sr.spec extraction-chromatography method for $^{90}$Sr determination, of low tolerance to the calcium content of the matrix.[25] In addition, extraction-chromatography columns are processed by physical adsorption of the extracting molecule on a inert polymer support, which is not satisfactory for use in radiopharmaceutical applications, because the extracting molecule can diffuse into the radionuclide solution used for radiolabelling.

The aim of this work was the development of a new extraction resin with high specificity for yttrium and lanthanides. The possibility of analyzing $^{90}$Sr in numerous environmental and biological samples by determining its daughter product $^{90}$Y was recently demonstrated. The method involves complexation of trivalent yttrium by three dipicolinate ligands to give an anionic species that is subsequently extracted on a polystyrene-based anion exchanger.[29,30] Thus, we speculated that anchoring dipicolinate ligands on a styrene matrix in an appropriate geometry would produce a polymer suitable for the specific recognition and extraction of yttrium. Consequently, the ion-imprinting technique was used to impress trivalent yttrium cations in a cavity formed by three dipicolinate entities bearing a vinyl function (Figure 1). We describe the synthesis of two novel vinyl derivatives of dipicolinic acid, HL1 and L2, their interaction with yttrium and lanthanide cations in solution and the solid-state properties of the isolated complexes. The last-named were used as templates for producing ion-imprinted resins that were tested for the separation of yttrium from high-calcium samples.

Results and Discussion

Synthesis and characterization of ligands HL1 and L2: Ligands HL1 and L2 were obtained from pyridine-2,6-dicarboxylic acid diethylester (1) and dimethyl ester (2), respectively (Scheme 1), synthesized from dipicolinic acid (dpa).[31] Vinylphenylamine was deprotonated in THF by addition of butyllithium and added to the esters, similarly to the procedure used for the addition of the lithium salt of diethylamine to ester 2.[32] In both cases, addition of the lithium salt of vinylphenylamine led to the mono- or disubstituted compound as the major product, depending on the number of equivalents added. Equimolar mixtures of vinylphenylamine and pyridine-2,6-dicarboxylic acid ester gave both the mono- and disubstituted products with the methyl ester in ratio 60:40, while the monosubstituted product 3 was the major product with the diethyl ester (92:8). Therefore, dimethyl ester 2 was preferentially used for the preparation of L2 and diethyl ester 1 for the synthesis of the monosubstituted precursor 3. To obtain HL1 in good yield, hydrolysis of 3 had to be performed under mild conditions; otherwise, the carboxamide moiety was also hydrolyzed upon heating and dpa was recovered.

In summary, HL1 was obtained by a three-step procedure in 65 % yield based on dpa, while L2 was isolated in two steps with 75 % yield. In [D6]DMSO, both HL1 and L1 display the expected eight signals arising from the aromatic and allylic protons, as well as a broad signal for the amide...
proton (Table 1). In CD$_3$CN, L$_2$ presents seven signals, consistent with the presence of a $C_2$ symmetry axis.

Single crystals of HL$_1$ suitable for X-ray analysis were grown from methanol and their structure elucidated (Figure 2). The crystal arrangement shows a network of very strong OH···O hydrogen bonds (O2···O3, 2.657(2) Å, O2/C0H2···O3 175.3°) between neighbouring molecules with formation of infinite chains along the $b$ axis. These chains are held together by weak N/C0H···O and CH···O interactions (for contact distances and angles, see Supporting Information). All bond lengths in HL$_1$ are standard and the ligand is nonplanar, as testified by the torsion angles N1-C1-C7-O3 (C0161.5(2)°) and C7-N2-C8-C9 (C0144.4(2)°), which indicate the relative position of the two aromatic rings. The presence of steric hindrance between O3 and H$_{13}$ and H$_{2A}$ and H$_9$ is revealed by the angles calculated between the following planes: (N1, C1–C5) and (C7, O3, N2) 19.8°, (N1, C1–C5) and (C8–C13) 35.5°, (C8–C13) and (C7, O3, N2) 54.6°.

Acidity constants of HL$_1$ were determined by spectrophotometric titration in H$_2$O/MeOH (99.5/0.5), by monitoring the spectral changes in the range 225–500 nm, from (H$_2$L$_1$)$^+$ at pH 2.0 (precipitation occurs at pH < 2.0) up to pH 12. Fitting the data to deprotonation Equilibria (1) and (2) yielded $pK_a$ = 2.8 ± 0.4 and $pK_a$ = 3.9 ± 0.4.

$$(H_2L_1)^+ = HL_1 + H^+ \quad K_{a1}$$

$$(HL_1)^+ = (L_1)^- + H^+ \quad K_{a2}$$

The first value corresponds to deprotonation of the carboxylic acid, and the second to deprotonation of the pyridinium nitrogen atom. Compared with dipicolinic acid ($pK_a$ = 2.38 ± 0.05 in H$_2$O/MeOH 99.5/0.5).

Table 1. Chemical shifts [ppm] and coupling constants for HL$_1$, NaL$_1$, [Y(L$_1$)$_3$] in [D$_6$]DMSO, and L$_2$, [Ln(L$_2$)$_3$]$^+$ (Ln = La, Y) in CD$_3$CN, at room temperature; see Scheme 1 for the numbering scheme of the protons.

<table>
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<th></th>
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<th>H$_2$</th>
<th>H$_3$</th>
<th>H$_4$</th>
<th>H$_5$</th>
<th>H$_6$</th>
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<td>8.6 Hz</td>
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<td>17.6 Hz</td>
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<td>6.26 d</td>
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<tr>
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<td>8.40 6.9 Hz</td>
<td>7.93 8.6 Hz</td>
<td>7.56 8.6 Hz</td>
<td>6.73 17.7+10.7 Hz</td>
<td>5.80 17.7 Hz</td>
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<td>8.23 7.8 Hz</td>
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<td>7.55 d</td>
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<td>8.6 Hz</td>
<td>8.6 Hz</td>
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<td>5.79 d</td>
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<td>8.37 7.8 Hz</td>
<td>7.76 d</td>
<td>7.44 d</td>
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<td>8.2 Hz</td>
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[a] HL$_1$ was deprotonated with 1 equiv of NaOD, dried and dissolved in [D$_6$]DMSO prior to measurement.

Figure 2. ORTEP view of the crystal structure of HL$_1$ showing the atom-numbering scheme; ellipsoids are represented at 50% probability.
2.16 and 4.76, or 2.03 and 4.49) the vinylic substituent substantially increases the acidity of the pyridinium nitrogen atom, while a concomitant decrease in the acidity of the carboxyl group is observed. The calculated distribution curves are shown in Figure 3: in aqueous solution at pH 7.4, the ligand is totally deprotonated.

Synthesis and characterization of the complexes: Complexes of HL1 and L2 with various lanthanides were synthesized either in methanol after deprotonation of HL1 or in acetonitrile in the case of L2, by mixing the ligand and partially dehydrated Ln(ClO4)3·nH2O (Ln = Y, La, Eu, Gd, Tb; n = 2.5–4) in stoichiometric quantities. In all cases a yellow precipitate of the desired [Ln(L1)3](ClO4)3·xH2O and [Eu(L2)3](ClO4)3 complexes was obtained in good yield (80–95%). The complexes with L1 are soluble in DMSO and in water containing 0.5 vol% of methanol. Complexes with L2 are hygroscopic; they are insoluble in water but they exhibit a solubility of 2 × 10⁻³ m in acetonitrile.

X-ray quality crystals of [Eu(L2)3](ClO4)3·2MeCN were grown by slow diffusion of tert-butyl methyl ether into a 10⁻³ m solution of the complex in acetonitrile. The compound crystallizes in the triclinic space group P1 and features discrete [Eu(L2)3]³⁺ cations and uncoordinated perchlorate anions. The crystal arrangement is characterized by rather strong hydrogen bonds between NH moieties, one acetonitrile molecule and the perchlorate anions (see Supporting Information). There are also weak interactions between most aromatic and allylic carbon atoms and perchlorate anions or the acetonitrile molecule not interacting with NH. Finally, weak interligand contacts take place through CH–π ring interactions but no direct π–π interaction is observed. In the [Eu(L2)3]³⁺ complex cation, the three ligand strands are analogously wrapped around the europium ion. The latter is nine-coordinate, with a slightly distorted tricapped trigonal prismatic coordination polyhedron close to D₃ vertex, in which the six oxygen atoms occupy the vertices and the three nitrogen atoms of the pyridine rings lie on the capping positions, forming an equatorially planar. The metal ion is located symmetrically with respect to the two planes defining the bases of the prism P1 (O1A, O1B, O2C) and P2 (O1C, O2A, O2B), with Eu–P1 and Eu–P2 distances of 1.726 (5) and 1.697(5) Å, respectively. Moreover, the deviation of the Eu ion from the equatorial plane defined by (N1A, N1B, N1C) is only 0.072(6) Å. Finally, the two distal planes P1 and P2 are almost parallel, with an interplanar angle of 1.8(1)°. The average Eu–O bond length is 2.414(8), which is identical, within experimental error, to that of 2.410(13) Å reported in the literature for the tris complex with pyridine-2,6-dicarboxylic acid bis(diethylamide). On the other hand, the mean Eu–N distance of 2.527(9) Å is somewhat shorter than that of 2.554(13) Å reported for the bis-amide complex.

The solution structure of the Y and La tris complexes was investigated by ¹H NMR spectroscopy (Table 1). In [D₆]DMSO, distinct signals were observed for free and coordinated L1⁺, contrary to solutions of the complexes with L2, which only showed the signals of the free ligand. That is, the

Figure 3. Distribution diagram for HL1, computed from the acidity constants given in the text.

Figure 4. Ball-and-stick representation of [Eu(L2)3](ClO4)3 with partial atom-numbering scheme.

Table 2. Selected bond lengths [Å] and angles [°] in [Eu(L2)3](ClO4)3·2CH3CN.

<table>
<thead>
<tr>
<th>Ligand a</th>
<th>Ligand b</th>
<th>Ligand c</th>
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<tbody>
<tr>
<td>Eu–O1</td>
<td>2.415(8)</td>
<td>2.406(8)</td>
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<tr>
<td>Eu–O2</td>
<td>2.417(7)</td>
<td>2.429(7)</td>
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<tr>
<td>Eu–N1</td>
<td>2.522(8)</td>
<td>2.528(7)</td>
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<tr>
<td>O1–Eu–N1</td>
<td>62.7(3)</td>
<td>63.2(3)</td>
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<tr>
<td>N1–Eu–O2</td>
<td>63.6(3)</td>
<td>63.2(3)</td>
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<tr>
<td>O1–Eu–O2</td>
<td>126.1(2)</td>
<td>126.3(2)</td>
</tr>
<tr>
<td>N–Eu–N</td>
<td>119.0(2)</td>
<td>118.6(2)</td>
</tr>
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strongly coordinating DMSO dissociates the complexes with 
\( L_2 \), while the competition with \( L_1 \) is in favour of the latter. 
The stability of the complexes of \( L_1 \) in DMSO allows the use of 
this solvent in the polymerization of the complexes to 
increase their solubility. On the contrary, this solvent cannot 
be used when imprinting polymers with \( L_2 \) complexes. 

The spectra of \([D_2]DMSO (L1)\) and \( CD_3CN (L2)\) solu-
tions containing a stoichiometric ratio \( Ln:L=1:3 \) (Table 1) 
display the same number of signals as the free ligands, and 
this points to the equivalence, on the NMR timescale, of 
the three ligand strands and to an averaged trigonal arrange-
ment of the complexes. The most shielded protons are those 
of the pyridine moiety, consistent with the fact that the pyri-
dine nitrogen atom is coordinated to the metal ion. On the 
other hand, the presence of the metal ion has little effect on 
the allylic protons, which lie far from the coordination 
sphere. In conclusion, the presence of aromatic vinyl carbox-
amide derivatives substituting the 2- and/or 6-position of the 
pyridine moiety does not affect the formation of 1:3 \( Ln:L\) 
complexes, which exhibit a trigonal symmetry, as reported in 
the literature for other dipicolinic acid derivatives.\(^{[35–37]}\)

The stability of the tris complexes was assessed by spec-
trophotometric titration of the ligands \((1.4 \times 10^{-4} \text{M})\) with 
lanthanide perchlorates \((10^{-3} \text{M})\). The absorption spectra of 
the ligands display three main bands located around 45900, 
38600 and 33000 \(\text{cm}^{-1}\) for \( L_1 \) in Tris-HCl buffer \((0.1 \text{m}, \text{pH} 7.4)\), and 50700, 38460 and 33000 \(\text{cm}^{-1}\) for \( L_2 \) in aceto-
nitrile. The more energetic bands are assigned to transitions 
mainly centred on the carbonyl groups and the middle band 
that at 33000 cm\(^{-1}\) is blue-shifted (ca. 1100 cm\(^{-1}\)) in the complexes with \( L_2 \). 
The band at 38460 is blue-shifted by about 1540 cm\(^{-1}\) in the 
complexes with \( L_1 \). In each case, 

\[
\begin{align*}
\text{Ln}^{3+} + \{Lx\}^{2-} & \rightleftharpoons \text{[Ln}(Lx)]^{3-(2-)} & \lg \beta_1 \\
\text{Ln}^{3+} + 2\{Lx\}^{2-} & \rightleftharpoons \text{[Ln}(Lx)]^{3-(4-)} & \lg \beta_2 \\
\text{Ln}^{3+} + 3\{Lx\}^{2-} & \rightleftharpoons \text{[Ln}(Lx)]^{3-(6-)} & \lg \beta_3 \\
\end{align*}
\]

where \( x = 1, i=1 \) and \( x = 2, i=0 \).

Since \( L_1 \) has one carboxylate group less than \( \text{dpa}^{2-}\), the 
first two successive stability constants are about one order 
of magnitude smaller than those found by Grenthe\(^{[38]}\) for di-
picolinate complexes \((\Delta \log K_{x} \approx 0.7, 0.8, \text{and } \Delta \log K_{y} \approx 1.0, 1.4\) 
for \( \text{Eu} \) and \( \text{Tb} \), respectively). On the other hand, the \( \lg \beta_i \) 
values are similar for the two series of complexes \((\Delta \log K_{x} \approx 0.4 \text{ and } \approx 0 \text{ for } \text{Eu} \text{ and } \text{Tb}, \text{respectively})\), which can be 
explained by the smaller charge borne by \( L_1 \) being compen-
sated by the fact that this ligand still interacts with a posi-
tively charged complex, while \([\text{Ln}(\text{dpa})_3]^+\) is negatively 
charged.

The \( \lg \beta_i \) values for the complexes with \( L_2 \) are 
identical, within experimental error, to those reported for 
the diethylamide-substituted ligand\(^{[39]}\) but the \( \lg \beta_i \) values are 
substantially smaller \((\Delta \log \beta_i \approx 1.2, 3.0, 3.2, \text{and } 2.0 \text{ for } \text{La}, \text{Eu}, \text{Tb, and Y}, \text{respectively})\). This points to a minor electri-
fic effect induced by the change in the amide substitu-
ts, while the substantial steric hindrance generated by the 
vinylenzene group makes coordination of the third ligand 
more difficult.

### Synthesis and characterization of polymers derived from \([Y(L_1)_3]\) and \([Y(L_2)_3](\text{ClO}_4)_3\):

Imprinted polymers were produced from divinylbenzene, 
allyl alcohol and azobis(iso-
butyronitrile). The amount of \([Y(L_1)_3]\) introduced into the 
polymer can reach 5 wt % if DMSO is added. For solubility 
reasons, imprinted polymers containing \([Y(L_2)_3](\text{ClO}_4)_3\) 
could not be synthesized in the same way. Pyridine had to 
be added in all cases for better solubility of the complex and 
it also acted as a porogen, while allyl alcohol was added to 
increase the hydrophilicity of the polymer. After imprinting 
the polymer with \([Y(L_1)_3]\) or \([Y(L_2)_3](\text{ClO}_4)_3\), yttrium was 
extracted under acidic conditions to provide the correspond-
ring metal-free yellow resins \(R-Y-L_1\) and \(R-Y-L_2\), respecti-
vely. Three reference polymers were prepared: resin \(R\), 
prepared from divinylbenzene and vinyl alcohol only, 
which does not contain any complex or ligand, and resins 
\(R-L_1\) and \(R-L_2\), with uncoordinated \(HL_1\) and \(L_2\), respecti-
vely. Furthermore a styrene polymer containing the highly lumines-
cent tris(dipicolinate) complex \([\text{Cs}_3\text{Eu}^{3+}(\text{dpa})_3]\) \(\text{[R-Eu-dpa]}\) 
was synthesized to test the uniformity of distribution of the 
complex centres in the resin. Under UV/Vis light, the red 
colour due to the luminescence of the Eu complex showed 
the homogeneity of the polymer (Supporting Information). 
When the \(\text{R-Eu-dpa}\) resin is washed with 0.1 m HCl, the 
luminescence disappears, consistent with removal of the EuIIc 
ations.

The ion-imprinted polymer with \([Y(L_1)_3]\) was analyzed with 
reflectance IR spectrometry. Its spectrum is compared in 
Figure 5 to those of polystyrene, free ligand, free complex
[Y(L1)] and metal-free resin R-Y-L1 (after acid treatment). The free ligand HL1 displays three characteristic bands at 1662, 1706 and 1745 cm\(^{-1}\), corresponding to vibrations of the pyridine double bonds and the carbonyl functions of the carboxyl and carboxamide groups (amide I), respectively. Upon coordination to yttrium in [Y(L1)], important shifts are expected for coordinated carboxylate,[40] the stretching frequencies are observed at 1545 cm\(^{-1}\) (\(v_s\)) and 1370 cm\(^{-1}\) (\(v_p\)). These values are close to those observed with dipicolinic acid, and \(\Delta \tilde{v} = 175\) cm\(^{-1}\) points to monodentate coordination of the carboxylate.[40] One band appears at 1272 cm\(^{-1}\) which can be attributed to coordinated pyridine. In parallel, the intense band observed in HL1 at 1523 cm\(^{-1}\), mainly corresponding to the C–N=O stretching vibration, is shifted to 1511 cm\(^{-1}\). Finally, one red-shifted and intense band at 1627 cm\(^{-1}\) is still observable, due to the pyridine double bonds. After polymerization of the complex, the resulting spectrum consists in a superposition of those of [Y(L1)] and polystyrene (cf. the bands at 1604, 1487, 1445 and 1370 cm\(^{-1}\) arising from the aromatic C–C bonds of styrene). The band at 1627 cm\(^{-1}\) is still observable, but slightly shifted to 1633 cm\(^{-1}\), and this indicates that Y\(^{III}\) remains coordinated and that the complex was not destroyed upon polymerization. After acid treatment to provide metal-free resin R-Y-L1, the two carbonyl vibrations and that of the pyridine moiety are recovered, at 1724, 1686 and 1633 cm\(^{-1}\), red-shifted by 20–30 cm\(^{-1}\) with respect to HL1. Additionally, the strong band at 1526 cm\(^{-1}\) is also recovered, so that the spectrum is close to a superposition of the spectra of polystyrene and the free ligand. To test the reversibility of complexation, resin R-Y-L1 was charged with europium: an IR spectrum close to that of the resin containing the yttrium complex was obtained, that is, the metal is complexed in the imprinted L1-containing cavity.

### Table 4. Ligand-centred absorption and emission properties of L2 and [Ln(L2)](ClO4)3 in CD3CN. L1 and the [Ln(L1)] in water at pH 7.4, 5 \(\times\) 10\(^{-4}\) M (Ln = La, Gd, Eu, Tb).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Absorption spectrum (\epsilon\text{ [cm}^{-1} \text{] (litr)})</th>
<th>(\epsilon_{\text{pp}}\text{[cm}^{-1} \text{]})</th>
<th>(\epsilon_{\text{pp}}\text{[cm}^{-1} \text{]})</th>
<th>(\tau \text{ [ns]})</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1</td>
<td>33000 (4.1); 38460 (4.0); 45870 (4.0)</td>
<td>25600</td>
<td>24550</td>
<td>27000</td>
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<tr>
<td>[La(L1)]</td>
<td>32400 (4.1); 39525 (4.2); 50600 (4.1)</td>
<td>25800</td>
<td>23400</td>
<td>26200</td>
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<tr>
<td>[Eu(L1)]</td>
<td>32400 (4.1); 39200 (4.2); 50600 (4.1)</td>
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<td>26400</td>
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<tr>
<td>[Gd(L1)]</td>
<td>32800 (4.1); 39100 (4.2); 50600 (4.1)</td>
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<td>23850</td>
<td>26500</td>
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<tr>
<td>[Tb(L1)]</td>
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<td>23800</td>
<td>26200</td>
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<tr>
<td>L2</td>
<td>33000 (4.5); 38500 (4.4); 50680 (4.9)</td>
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<td>22700</td>
<td>26500</td>
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<td><a href="ClO4">La(L2)</a>3</td>
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<td>22300</td>
<td>21100</td>
<td>24700</td>
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<tr>
<td><a href="ClO4">Eu(L2)</a>3</td>
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<td>21500</td>
<td>24800</td>
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<tr>
<td><a href="ClO4">Gd(L2)</a>3</td>
<td>32780 (4.4); 38950 (4.4); 50530 (4.9)</td>
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<td>21600</td>
<td>24600</td>
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<tr>
<td><a href="ClO4">Tb(L2)</a>3</td>
<td>32550 (4.5); 38800 (4.3); 50680 (4.9)</td>
<td>22900</td>
<td>21800</td>
<td>24400</td>
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</tbody>
</table>

[a] Maxima of the band envelopes at 295 K. [b] From fluorescence spectra at 295 K; energies are given for the maxima of the band envelopes (in italics), and 0-phonon transitions are marked with asterisks. [c] From phosphorescence spectra of frozen solutions at 77 K. [d] Lifetimes in frozen solutions at 77 K.
symmetry-forbidden in this context consistent with the fact that it is transition is not detected, consistent with the relative area of the $\pi^*\pi$ and $\pi^*\pi$ emissions at 77 K, remains sizeable; 60% for $\text{L1}$ and 55% for $\text{L2}$.

The lifetimes of the $\pi^*\pi$ states are short, but similar given the different solvents used (320 $\mu$s for $\text{L1}$ and 250 $\mu$s for $\text{L2}$). After complexation with $\text{La}^{3+}$, $\text{Gd}^{3+}$, $\text{Eu}^{3+}$, or $\text{Th}^{3+}$, these bands are slightly shifted (see Table 4). In addition, the $\text{Eu}^{3+}$ and $\text{Th}^{3+}$ complexes display the characteristic narrow emission lines of the metal ions that reflect $\pi^*\pi \rightarrow \mathrm{Ln}$ energy transfer. This is more efficient with $\text{Eu}^{3+}$, since no triplet phosphorescence was observed with this ion, although some singlet-state emission was still detected. The luminescence decays at 77 K are single exponential functions and to some singlet-state emission was still detected. The luminescence is very similar, both with respect to relative intensities and crystal-field splitting, that is, polymerization induces only minor changes in the $\text{Eu}^{3+}$ environment. It is noteworthy that the emission bands are not broadened, consistent with a homogeneous distribution of the sites. The metal-ion environments in the cavities of the imprinted polymers were probed by high-resolution luminescence of $\text{Eu}^{3+}$.[42–44] The yttrium-free resins were treated in batch mode with aqueous solutions of europium chloride at pH 4 and analyzed by luminescence. The results were compared with those obtained for the parent complexes $[\text{Eu(\text{L1})}]_3$ and $[\text{Eu(\text{L2})}]_3(\text{ClO}_4)_3$ (Figure 7, Table 5). At 77 K, the ligand-field splitting of the $[\text{Eu(\text{L1})}]_3$ levels can be interpreted in terms of $D_2$ symmetry around the $\text{Eu}^{3+}$ ion.[45] The $D_0 \rightarrow F_0$ transition is not detected, consistent with the fact that it is symmetry-forbidden in this point group. There are three main transitions to the $F_1$ level almost equally spaced ($\Delta E = 92$ and 74 cm$^{-1}$), corresponding to $A \rightarrow B_1$, $B_2$, $B_3$ transitions allowed in $D_2$ symmetry. The $D_0 \rightarrow F_1$ transition displays two main components and a smaller (possibly split) one on the low-energy side consistent with the three allowed transitions in $D_2$; in addition, a very faint, vibronic component appears at 16119 cm$^{-1}$. Finally, the $D_0 \rightarrow F_1$ transition displays seven components, while six are predicted theoretically ($A \rightarrow B_1$, $B_2$, $B_3$). The emission spectrum of $\text{R-Eu-L1}$ is very similar, both with respect to relative intensities and crystal-field splitting, that is, polymerization induces only minor changes in the $\text{Eu}^{3+}$ environment.

The luminescence spectrum of $[\text{Eu(\text{L2})}]_3(\text{ClO}_4)_3$ is much simpler, with essentially one main component for $D_0 \rightarrow F_1$ transitions relative to the magnetic dipole $D_0 \rightarrow F_1$ transition, measured at 77 K on solid-state samples, and identified crystal-field sublevels [cm$^{-1}$] of the $F_1$ manifold ($F_0$ is taken as the origin); $\varepsilon_{\nu} = 36630$ cm$^{-1}$; $\nu$ = vibronic.

<table>
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<td>1.34</td>
<td>0.01</td>
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<tr>
<td>$\text{R-Eu-L1}$</td>
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<td>$[\text{Eu(\text{L2})}]_3^{+*}$</td>
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<td>0</td>
<td>0.30</td>
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<tr>
<td>$\text{R-Eu-L2}$</td>
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<td>1.96</td>
<td>0.001</td>
<td>0.36</td>
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</table>

<table>
<thead>
<tr>
<th>Compound</th>
<th>relative intensities</th>
<th>crystal-field sublevels</th>
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<tbody>
<tr>
<td>$[\text{Eu(\text{L1})}]_3$</td>
<td>0 304, 396; 470 968, 1010, 1110, 1146(v) 1852, 1913</td>
<td>2679, 2730, 2810, 2856, 2897, 2967</td>
</tr>
<tr>
<td>$\text{R-Eu-L1}$</td>
<td>0 310, 396, 452 967, 1015, 1114, 1151, 1386</td>
<td>2669, 2665, 2720, 2829, 2866, 2957, 3050</td>
</tr>
<tr>
<td>$[\text{Eu(\text{L2})}]_3^{+*}$</td>
<td>0 384 994, 1099, 1140(v) –</td>
<td>2677, 2833, 2850, 3050</td>
</tr>
<tr>
<td>$\text{R-Eu-L2}$</td>
<td>0 310, 384, 537 972, 1004, 1125</td>
<td>2669, 2716, 2821, 2850, 3038</td>
</tr>
</tbody>
</table>
Ion-Imprinted Polystyrene Resins

Yttrium extraction: Distribution coefficients were determined in batch mode with 500 mg of resin (170–230 mesh) at pH 4 in H₂O/EtOH 95:5 [Eq. (6)].

\[
D = \frac{c_f - c_i}{c_i} \frac{V}{m}
\]

where \(c_i\) is the initial concentration of the cation, \(c_f\) the final concentration after equilibrium is reached, \(V\) the volume of the solution and \(m\) the quantity of resin. The distribution coefficient of R-Y-L1 relative to yttrium is 570 mL·g⁻¹, which is significantly larger than that of resin R-L1 (\(D = 35 \text{ mL} \cdot \text{g}^{-1}\)), and the template effect is characterized by a \(D_{\text{R-Y-L1}}/D_{\text{R-L1}}\) ratio of 16. The “blank” polymer (resin R), resin R-L2 and resin R-Y-L2 do not extract any yttrium under the given experimental conditions (\(D = 0 \text{ mL} \cdot \text{g}^{-1}\)). Slight extraction of yttrium by R-L1 is probably due to the presence of carboxyl groups in the resin, while R-L2 is devoid of such groups. The lack of extraction of yttrium by R-Y-L2 may be explained by the presence of perchlorate anions during the imprinting process of the resin, which are further removed upon acid washing.

Batch experiments were also carried out to determine the capacity of resin R-Y-L1 to retain yttrium cations. Three runs involving 1 g of the resin and 20 mg of yttrium yielded a capacity of 8.9 ± 0.2 mg g⁻¹. Thus, the resin is able to extract macroquantities of yttrium when the pH is kept above 2.5. An estimate based on the quantities introduced in the synthetic procedure and on the quantity of extracted yttrium, leads to 44% of the complexation sites being active, which means that the porosity induced by DMSO and the hydrophilicity induced by allyl alcohol are optimum. In column experiments designed to determine the best extraction pH of the resin, 100% of the extraction capacity of the resin is achieved at pH 3.0. At pH 2, 60% extraction is reached, while at pH 1.0, only 15% of the extraction capacity is obtained. Thus, extraction of yttrium cations can be achieved at an acidic pH very suitable to avoid precipitation of hydroxide species, while in many literature reports extractions were conducted at a pH above 6, which reduces the validity of the methods. The acidic character of cations with high charge density (e.g., lanthanides or Y(III)) competes effectively with protons for complexation to the carboxyl groups of the dipicolinic moieties at pH < 3.0. Rapid extraction kinetics are required due to the high elution rate used in column extraction chromatography. Two batch experiments carried out with 1 g of resin showed that the extraction kinetics are indeed very fast: 100% of the yttrium capacity is reached after only 10 min of contact of the resin with the spiked solution (10 mg Y, 50 mL, \(t_{1/2} = 1.7\) min, Figure 8a). Say et al. obtained an equilibrium time of 60 min in the extraction of copper(II) ions with an imprinted meth-
acrylate polymer[3] and Biju et al. demonstrated that they could extract 100% of dysprosium from an aqueous solution at pH 6 in less than 5 min with an imprinted polystyrene polymer.[16] For extraction of Y[III] or Ln[III] ions from environmental samples or for production of medical radioactive sources, for example, 89Y, elution profiles must show complete extraction of the metal ion, followed by a total elution from the column with a very small volume of the eluent solution. Figure 8b displays the results obtained for chromatographic experiments carried out on 2 g of R-Y-L1, starting with 20 mL of solution at pH 4, spiked with 10 mg of yttrium. The flow rate was 1 mL min⁻¹ and the collected fractions amounted to 3 mL. Extraction of yttrium is clearly quantitative and the elution volume can be kept very small by using dilute hydrochloric acid: no significant change in the elution profile was noted when 1, 0.1 or 0.05 M aqueous HCl was used to elute Y[III] from the column. Such dilute media are of interest in view of medical radiolabelling applications. To test whether the resin can be used for preparation of medical-grade 89Y, for example, without strontium and zirconium, the elution profile of a solution containing carrier-free 85Sr, 89Y and 95Zr was determined (Figure 9):

\[ D_{\text{Y}} = \frac{S_{\text{Y}}}{S_{\text{Ln}}} \]

where \( D_{\text{Y}} \) is the distribution coefficient of yttrium, and \( S_{\text{Ln}} \) is the distribution coefficient of the lanthanide ion. Selectivity for the heavier lanthanides (Figure 8c) is demonstrated by the larger \( S \) values for the lighter La[III] and Nd[III] ions. Selectivity was also tested in an experiment on a chromatographic column (2 g of R-Y-L1). Pairs of Y/Ln ions were extracted from 20 mL of solution at pH 4, and the selectivity was calculated as the ratio of the percentage of extracted Y[III] to the percentage of extracted lanthanide. The obtained \( S \) values range from 6 for Y/La to 0.5 for Y/Yb, and the selectivity sequence is La < Nd < Eu, Gd, Tb, Yb. Furthermore, the ion-imprinting effect, as measured by the increase in capacity when comparing R-Y-L1 with blank R-L1, is large: a ratio of up to 16 was obtained. For comparison, Vignau et al. obtained a value smaller than 2 for Gd/La in the case of a resin imprinted with a 1:1 complex.[16] This could indicate that the increase in selectivity displayed by the latter resin is primarily driven by affinity, while in our case it is due to a size effect.

Finally, selectivity of R-Y-L1 for Y[III] over Ca[II] and Sr[II] was tested by batch extraction. For 0.5 g of resin, \( D = 0 \) mL g⁻¹ for both alkaline earth metal ions. Additionally, two 10 mg samples of Y[III] were extracted from 5 g samples of milk ash in 200 mL water on 2 g of R-Y-L1: Y[III] recovery amounted to 72 ± 4%. Since milk ash contains large amounts of potassium, calcium, and magnesium, this demonstrates that the resin is able to extract very small quantities (milligrams) of yttrium from macroquantities (grams) of alkali and alkaline earth metals. A much larger amount of resin is needed for a similar separation with a resin such as Dowex AG50w, for which the stability constant of the resin-metal complex plays a major role in the separation process. Moreover selective complexing agents such as ethylenediaminetetraacetic acid (EDTA) and \( \alpha \)-hydroxyisobutyric acid (\( \alpha \)-HIBA) are often necessary to improve the separation factor.[49,50] Thus ion-imprinted polymers with predefined cavities allowing size exclusion can improve the separation of metal cations. In this context, Rao et al. were able to separate Er[III] from Y[III], Dy[III], Tb[III] and Ho[III] by solid-phase extraction using ion-imprinted polymer particles.[51]

### Conclusion

We have demonstrated that imprinting a polymer with neutral \( [\text{Y(L1)}]_n \) complex, followed by acid demetallation, leads to a resin with high selectivity for Y[III] and heavy Ln[III] ions over calcium, strontium and potassium. Size exclusion of the lighter lanthanides from the preorganized cavity is thought to be the mechanism responsible for the observed selectivity, since neither calcium nor strontium was extracted by the imprinted resin in blank experiments with these ions. The obtained ion-imprinting effect stems from the rigid geometry imposed by the three dipicolinate-based ligand strands, which is maintained upon polymerization. The larger lanthanide cations such as La[III] and Nd[III] are prevented from entering the cavity tailored for Y[III], while the size mismatch is minimal for the heavier Ln[III] ions. Overall, the reported

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**Figure 9.** Elution profile of the radiotracer experiment on 200 mg of R-Y-L1 resin. Black bars: 89Y, hatched bars: 90Zr, white bars: 85Sr (from 0 to 7 mL: 0.001 M HCl, from 7 to 9 mL: 1 M HCl).

---

\[ \frac{\text{log}(C_{\text{Y}})}{\text{log}(C_{\text{Ln}})} \]

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data open the way for the use of such resins for the production of medical-grade $^{90}$Y, which necessitates a very high $^{89}$Sr decontamination factor, as well as for the analysis of the highly toxic radiotriontium $^{90}$Sr in milk and other foods by measurement of its daughter product $^{90}$Y. The production of medical-grade lanthanides could also benefit greatly from this size-exclusion, imprinted-polymer technique. Further examples of radiotracer experiments and detailed analytical data obtained with the ion-imprinted resin based on $[\text{Y(LI)}_3]$ will be published elsewhere.$^{[52]}$

**Experimental Section**

**Materials and general methods:** Analytical-grade chemicals were obtained from Merck, Acros, Fluka or Carlo-Erba. Divinylbenzene (Fluka) contained a 50:50% mixture of isomers. Ultrapure water was supplied by an SG Ultra-Clear UV apparatus. Reactions were conducted under inert atmosphere with standard Schlenk and dry-box techniques. THF was distilled from Na benzophenone, and acetonitrile from CaH$_2$. Stock solutions of Ln(ClO$_4$)$_3$·$n$H$_2$O ($n = 2.5$–$4$; Ln = Y, Eu, Tb, La, Gd) were prepared from lanthanide oxides$^{[39]}$ (99.99%, Rhône Poulenc) and the corresponding acid; concentrations were determined by complexometric titrations.$^{[40]}$ Elemental analyses were performed by Dr. Eder, Microchemical Laboratory of the University of Geneva.

**Caution!** Perchlorate salts of complexes with organic ligands are potentially explosive and should be handled in small quantities and with adequate precautions.$^{[39]}$

$^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker Avance DRX 400 spectrometer at 25°C. Chemical shifts are given in ppm versus TMS. Positive-mode ES-MS spectra of 10$^{-5}$–10$^{-6}$ m solutions in CH$_2$CN or MeOH/H$_2$O were obtained with a Finnigan SQ 710C spectrometer calibrated with horse myoglobin (capillary temperature 200°C, acceleration potential 4.5 kV, ion spray voltage 4.6 kV).

**Photophysical measurements:** UV/Vis absorption spectra were measured on a Perkin-Elmer Lambda 900 spectrometer using quartz Suprasil cells of 0.2 and 1 cm path length. Spectrophotometric titrations were performed with a J&M diode-array spectrometer (Tidas series) connected to a PC. Spectra were recorded in a 1 cm cell temperature (25.0 ± 0.1°C) glass-jacketed vessel at $\mu = 0.1$ m (KCl(aq) for HL$_1$ and Et$_3$NCI in acetonitrile for L$_2$). In a typical ligand titration, 50 mL of L was titrated with freshly prepared NaOH solutions at different concentrations (4, 1, 0.1 and 0.01 m). After each addition of base, the pH of the solution was measured by a KCl-saturated electrode, and UV/Vis absorption spectra were recorded with a Hellma optrode (optical path length 0.1 cm) immersed in the thermostated titration vessel and connected to the spectrometer. Factor analysis$^{[50]}$ and mathematical treatment of the data were performed with the SPECFIT program.$^{[51,52]}$

Low-resolution luminescence measurements were recorded on a FluoroLog FL3-22 spectrometer from Horiba-Jobin-Yvon-Spec. Emission and excitation spectra were measured in 1 cm quartz Suprasil cells at room temperature (25.0 ± 0.1°C, FL-1027 thermostated cell holder) and corrected for the instrumental function. Phosphorescence lifetimes were measured with the instrument in time-resolved mode, on frozen glycerol/water (10:90) or acetonitrile solutions at 77 K in a quartz capillary or a 1 cm Suprasil cell. They are averages of at least three independent measurements performed by monitoring the decay at the maxima of the emission spectra and enforcing a 0.03–0.05 ms time delay. All the decays were monoexponential and were analyzed using Origin 7.0.

**X-ray crystallography:** Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a 10$^{-3}$ m solution of [Eu(L$_2$)$_3$](ClO$_4$)$_3$·2CH$_3$CN in MeCN. Data were not corrected for absorption. Structure solution and refinement as well as molecular graphics and geometrical calculations were performed with the SHELXTL software package, release 5.1.$^{[37]}$ Structures were refined by full-matrix least-squares techniques on $F^2$ with all non-H atoms anisotropically defined. H atoms were placed in calculated positions using the riding model. In the case of [Eu(L$_2$)$_3$](ClO$_4$)$_3$, the disorder exhibited by two perchlorate anions and the solvent was treated by means of the split model and applying geometrical restraints. Data are reported in Table 6.

<table>
<thead>
<tr>
<th>Table 6. Crystal data and structure refinement for HL$_1$ and <a href="ClO$_4$">Eu(L$_2$)$_3$</a>$_3$.</th>
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</table>

CCDC-286910 and -286911 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

**Synthesis of the ligands (Scheme 1):** Pyridine-2,6-dicarboxylic acid diethyl ester (1) and pyridine-2,6-dicarboxylic acid dimethyl ester (2) were synthesized according to Crystal et al.$^{[53]}$

6-(4-Vinylphenylcarbamoylpyridine-2-carboxylic acid ethyl ester (3): Vinylphenylamine (95.9%, 5.4 g, 44 mmol) was dissolved in anhydrous THF (500 mL) under N$_2$. To this stirred solution, n-butyllithium (1.6 m in pentane, 27.5 mL, 44 mmol) was slowly added at RT. The yellow solution was stirred for 30 min and then added dropwise to a solution of 1 (10 g, 44.8 mmol) in THF (150 mL). The orange-brown solution was stirred overnight under N$_2$, and the solvents were removed by evaporation. The
brown residue was dissolved in CH2Cl2 (300 mL) and washed with water (2 × 300 mL), the organic layer dried over Na2SO4 and the solvent removed. The crude product was dissolved in diethyl ether (250 mL), yielding L2 as a precipitate (1 g, 8%). After evaporation of the filtrate, the solid was obtained as pale yellow solid (10 g, 68%). H NMR (400 MHz, DMSO-d6): δ = 10.09 (br, 1H, NH), 8.26 (d, J = 7.8 Hz, 1H), 8.06 (d, J = 7.7 Hz, 1H), 7.89 (d, J = 7.8, 7.7 Hz, 1H), 7.45 (d, J = 8.6 Hz, 2H), 7.26 (d, J = 8.6 Hz, 2H), 6.63 (d, J = 17.7, 10.9 Hz, 1H), 5.72 (d, J = 17.7 Hz, 1H), 5.26 (d, J = 10.9 Hz, 1H), 4.52 (q, 2H, OCH2), 1.49 (t, 3H, CH3); elemental analysis (%) calced for C16H14N2O3·0.25H2O: C 51.97, H 3.62, N 7.49; found: C 51.66, H 3.85, N 7.94; elemental analysis (%) calcd for C69H57Cl3N9O18Y: C 55.42, H 3.84, N 8.43; found: C 55.30, H 3.46, N 8.04.

Synthesis of Ln(III) and Ln(L2)(ClO4)3 (Ln = La, Eu, Gd, Tb) These complexes were synthesized according to the experimental procedures described above. Elemental analysis (%) calcd for La(1.25 H2O): C27H23NO10·1.25H2O: C 56.11, H 3.71, N 8.73; found: C 56.13, H 3.91, N 8.36; elemental analysis (%) calcd for Eu(1.25H2O): C27H23NO10·1.25H2O: C 56.2, H 3.65, N 8.65; found: C 55.62, H 3.81, N 8.47; elemental analysis (%) calcd for Gd(1.7H2O): C27H23NO10·1.7H2O: C 56.3, H 3.57, N 8.65; found: C 55.62, H 3.66, N 8.44; elemental analysis (%) calcd for Tb(1.7H2O): C27H23NO10·1.7H2O: C 55.3, H 3.56, N 8.64; found: C 55.55, H 3.74, N 8.44; elemental analysis (%) calcd for Ce(1.7H2O): C27H23NO10·1.7H2O: C 55.8, H 3.98, N 7.73; found: C 50.50, H 3.96, N 7.57; elemental analysis (%) calcd for Tb(2H2O): C27H23NO10·2H2O: C 51.75, H 3.84, N 7.87; found: C 51.66, H 3.85, N 7.94.

Synthesis and characterization of the yttrium resin: Resin R-Y-L1 Complex [Y(L1)] (1 g, 1.12 mmol), DMSO (3 mL), divinylbenzene (3 mL), pyridine (3 mL), allyl alcohol (3 mL) and of azobis(isobutyronitrile) (25 mg) were introduced into a tube containing a magnetic stirrer. The tube was purged under vacuum and filled with argon. It was placed in an ultrasonic bath and sonicated for 15 min under argon to remove any trace of oxygen. Caution must be taken never to stop agitatin when de-gassing the polymer mixture, otherwise a sticky precipitate appears which can only be redissolved with difficulty. The tube was then sealed and placed in an oil bath at 85°C for 12 h. Polymerization was conducted with vigorous stirring to allow for good dispersion of the resin into the polymer. Finally, the tube was crushed; the crude product washed with methanol and then coarsely crushed in a mortar. The bulk product was washed successively in methanol, ethanol and water/ethanol 90/10 several times. Finally, the product was washed with 5m HCI to remove the yttrium template, then several times with water and allowed to dry. The yttrium-free resin R-Y-L1 was finely ground in a mortar and the fractions 60–120 mesh, 120–170 mesh, 170–230 mesh and > 230 mesh were separated with a set of sieves.

The other resins were synthesized by using a slightly modified procedure: R-Y-L2 was obtained from [Y(L2)(ClO4)3] (1 g, 0.67 mmol) and without DMSO; for resin R, no complex was added; for resin R-L1, 900 mg, 3.26 mmol) was added instead of [Y(1.25L1)]; for resin R-L2, R-Y-L2 (740 mg, 2 mmol) was added instead of [Y(1.25L2)]. For resin R-Eu-L1, 468 mg, 0.448 mmol) was added instead of [Y(1.25L1)].

Analytical measurements: Chromatographic elution profiles and yttrium yield were determined by atomic absorption (410.2 nm) with a Perkin Elmer 410 atomic spectrometer using a N2O-acetylene flame. Calcium (422.7 nm) and strontium (460.7 nm) were determined in the same way using an air/acetylene flame. In the selectivity experiment Y, La, Nd, Eu, Gd, Tb and Yb were determined by atomic emission with a Perkin
Elmer ICP-AES spectrometer Optima 2000 DV. Multiple-wavelength analysis was used. Chromatographic columns were made of 2 g of the yttrium resin in a 6 mL Supelco column 57242. Supelco no. 57273-U column adaptor and Ismatec IPS-12 peristaltic pump were used to pump the solutions into the column.

**Column preparation:** The resin (2 g, 60–120 mesh) was dispersed in water containing 5% ethanol and stirred for 15 min before introducing the mixture into a 6 mL Supelco column; a Teflon frit was added on top of the resin bed. A Supelco no. 57273-U tube adapter was clamped to the column to allow utilization of the column with a peristaltic pump (Ismatec IPS-8), overpressure being necessary for the solution to pass through the column. Elution profiles were recorded with 20 mL of a solution containing 10 mg of yttrium at pH 4. Fractions of 3 mL were collected and yttrium content determined by atomic absorption.

**Batch experiments:** 0.5 g of resin (170–230 mesh) was suspended in water (50 mL) containing 5% ethanol and the pH was adjusted to 4. Y(10 mg), Ca(10 mg), Sr(10 mg) or Y/Ln pairs (10 mg/10 mg) were introduced as standard chloride solutions at pH 4. After equilibrium was reached (ca. 20 min), an aliquot of the supernatant (1 mL) was sampled and filtered (0.45 μm) in a syringe, and the Y or Ln content determined by atomic absorption or ICP-AES. Kinetic experiments were performed in the same way; aliquots of 1 mL were taken after 0.5, 1.5, 3, 5, 7, 10, 20 and 40 min. Errors in batch experiments were estimated to be 5%, mainly due to AA or ICP-AES determination and loss in filtration.

**Radiotracer experiment:** All experiments were performed with 22Na (94028±950 Bq/mL) and 85Sr (148000±376 Bq/mL) and 88Y (1700±2200 Bq/mL) (Eds.: A. Sigel, H. Sigel), Marcel Dekker, New York, Basel, 1990.

**Extraction of yttrium from milk samples:** Milk ash (5 g) was dissolved in 32% HCl (20 mL) and YCl3 was added (10 mg). The mixture was heated to allow slow evaporation of the acid. When the volume reached about 5 mL, water was added (200 mL). If necessary, the solution was filtered. 2.5 N NaOH was added to raise the pH as close as possible to 3.0 while avoiding precipitation of calcium phosphate. The solution was pumped into the column (2 g resin) at a rate of 1 mL/min. After washing the column with water (20 mL), YIII was eluted with 1 M HCl (10 mL) and the yield was determined by atomic absorption spectrometry.

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