

Ionic Liquid-type Crown Ether as a Novel Medium for a Liquid/Liquid Extraction of Radioactive Metal Ion $^{85}\text{Sr}^{2+}$

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1,13-Dichloro-4,7,10-trioxatridecane (2-[2-(1-chloro-2-ethoxy)ethoxy]ethyl chloride) (**3a**) was synthesized by a chlorination of 1,13-dihydroxy-4,7,10-trioxatridecane (triethylene glycol). And it was treated with imidazole and sodium ethoxide to give the 1*N*,1*N'*-tris(oxoethylene)-diimidazole (**3b**), which was then converted to ionic liquid-type crown ether (ILCE) **3** with a reaction with 1,9-dichloro-3,6-trioxaoctane (**2a**). Further, the anion of ILCE was exchanged by an anion-exchange method. Ultimately, we developed a very efficient synthetic pathway for ILCEs **1–4** which have various physical and chemical characteristics by a modification of the polyethylene glycol chain length and anions. $^{85}\text{Sr}^{2+}$ was successfully extracted into the [(3,2)*O*_{Et}Im][Cl] (**3**) phase, but it was not extracted into the [(2,2)*O*_{Et}Im][Cl] (**1**), [(3,3)*O*_{Et}Im][Cl] (**2**), and [(4,3)*O*_{Et}Im][Cl] (**4**) phases.

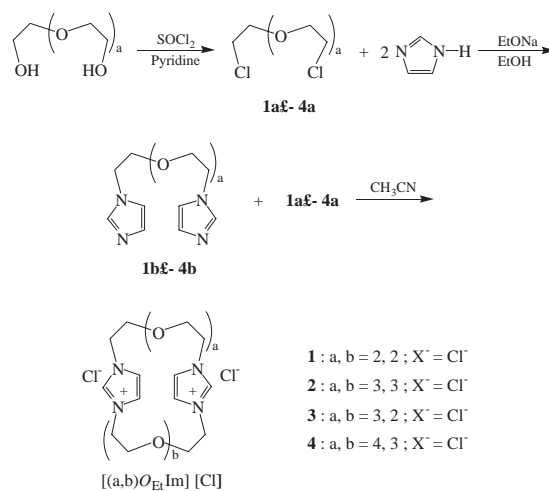
The interest for radiopharmaceuticals for the treatment of serious illness such as cancer and rheumatism has increased during the last decade. Radioisotopes of ^{90}Sr , ^{186}Re , ^{153}Sm , ^{90}Y , and ^{166}Ho are currently used in the routine practice of medical clinics. $^{89}\text{Sr}^{1}$ is a radionuclide which has been used for a palliative treatment of bone cancers and a treatment of prostate cancer. ^{90}Sr is a parent nuclide of ^{90}Y -generator which is being used as a radiotherapeutic nuclide.² Accordingly, many methods for these radioisotope extractions have been proposed with the growth of nuclear medicine. The $^{89/90}\text{Sr}$ can be extracted by using crown ethers. The crown ethers 18-crown-6 (18C6), dicyclohexano-18-crown-6 (DCH18C6), and 4,4'-(5')-di(*tert*-butylcyclohexano)-18-crown-6 (DtB18C6) have been studied for an extraction of Sr^{2+} from aqueous solutions.³ In the absence of an extractant, the distribution ratio for the metal ion indicates a strong preference for the aqueous phase. In a typical liquid/liquid extraction experiment, the crown ether resides in the hydrophobic extraction phase and serves to dehydrate and complex the metal ions while removing them from the aqueous phase.^{4,5} To enhance the efficiency of such a process, an organic solvent is selected to sustain the biphasic system while maximizing the hydrophobic and complexing properties of the extracting phase. However, the volatile organic compounds (VOCs) commonly employed in traditional liquid/liquid separations can have high hazard ratings and low flash points, indicating associated health and safety concerns. While liquid/liquid separations by utilizing VOC diluents have extensive applications in industry from chemical synthesis to an hydrometallurgy, the end result of such practices often generates volumes of contaminated solvent. Ending the reliance on separations that consume large quantities of VOCs has become a target area for an emphasis in the development of "Green" industrial processes that are inherently safer and are less polluting.^{6–10} In recent years, ionic liquids have

attracted much attention as recyclable media for an organic synthesis and a solute–solvent interaction.^{3,11–13} They are considered as green solvents since they are non-volatile, non-flammable, non-toxic, thermally stable, and recyclable. Limited solubility of ionic species in nonionic organic solvents is the main problem associated with conventional solvent extractions. Therefore, a synthesis of new ionic liquid-type crown ethers was performed for a liquid/liquid extraction of metal ions. The new crown ethers have a large polyoxyethylene ring, which is capable of interacting with metal ions to produce a complex of associates. Certain modifications can be made to produce a molecule designed for optimal results for specific applications. The goal is a development of novel sequestering agents to achieve the extreme selectivity required to extract specific radionuclides.

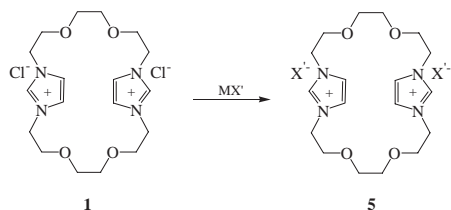
Polyethylene glycol in benzene was treated with pyridine and thionyl chloride to give compounds **1a–4a**. A solution of imidazole (0.20 mol) in 100 mL of absolute ethanol was treated with compounds **1a–4a** (0.10 mol) and sodium ethoxide. The mixture was stirred and refluxed for 6 h to give compound **1b–4b**. And compound **1b–4b** (0.20 mol) in 250 mL of anhydrous acetonitrile was treated with 0.20 mol of compounds **1a–4a** to give compound **1–4** in good yields (Scheme 1). Instrumental analyses confirmed the chemical structure of the target compounds **1a** and **3**.¹⁴

The ring size of the ILCEs can be regulated by an increase of the ether chain length.

Physical characteristics of ILCE can be regulated by the anion-exchange reactions. Sodium trifluoroacetate was added to a solution of the [(2,2)*O*_{Et}Im][Cl] (**1**) prepared above in acetone. This mixture was stirred at room temperature for



Scheme 1. Synthesis of [(a,b)*O*_{Et}Im][Cl].



Scheme 2. Synthesis of ILCE by anion-exchange reaction.

24 h. Other anion substituted ILCEs can be prepared in the same way as 5 from AlCl_4^- , Al_2Cl_7^- , BF_4^- , SbF_6^- , NO_3^- , HSO_4^- , CF_3SO_3^- , and $(\text{CF}_3\text{SO}_3)_2\text{N}^-$ (Scheme 2).

^{85}Sr was produced at the HANARO research reactor (30 MW) installed at the Korea Atomic Energy Research Institute by a neutron irradiation of a capsulated $^{84}\text{SrCO}_3$ target for 24 min at a neutron flux ($2.5 \times 10^{13} \text{ n/cm}^2 \cdot \text{s}$). And it was cooled for 24 h and dissolved in deionized water and 1 M nitric acid. The radionuclidic purity of the ^{85}Sr was estimated by a γ -ray spectrometry (GEM-10175 HPGe Detector coupled to a Multi-Channel Analyzer, ORTEC, Oak Ridge, TN, U.S.A.). A typical γ -ray spectrum obtained from the HPGe detector shows photopeaks due to the γ -rays of ^{85}Sr and $^{87\text{m}}\text{Sr}$. The 514.0 and 388.4 keV photopeaks were used for the assay. The initial specific activity of ^{85}Sr was 189 Bq/mg. The radioactivity was measured by using an ionizing chamber (Capintec 15R, BIODEx Atomlab 200, NY, U.S.A.) by setting the calibration value for ^{85}Sr which was corrected and calibrated by the manufacturer.

Metal ion distribution ratios were determined by mixing 1 mL of ILCE and 1 mL of aqueous phase followed by vortexing (2 min) and centrifuging (2000 g, 2 min) to equilibrate the phases. Addition of the metal ion tracer (ca. 407 Bq, 5 μL) was followed by two intervals of a vortexing (2 min) and a centrifuging (2000 g, 2 min) to ensure that the phases were fully mixed and separated. The phases were separated and dispensed into shell vials from which 100 μL of each phase was removed for a radiometric analysis. Because equal volumes of both phases were removed for an analysis, the distribution ratio (D) for the metal ions was determined as follows:

$$D = \frac{\text{Activity in the ILCE lower phase}}{\text{Activity in the aqueous upper phase}} \quad (1)$$

Each experiment was done in duplicate and the results agreed to within 5%.

$^{85}\text{Sr}^{2+}$ was successfully extracted into cyclo- $\{1\text{N},1\text{N}'\text{-}[(3,6,9\text{-trioxa})\text{-}1,11\text{-undecyl}]\text{-}\{3\text{N},3\text{N}'\text{-}[(3,6\text{-dioxo})\text{-}1,8\text{-octyl}]\text{-}\}$ diimidazolium chloride $\{[(3,2)\text{O}_{\text{Et}}\text{Im}][\text{Cl}]\text{ (3)}\}$ phase, but it was not extracted into $[(2,2)\text{O}_{\text{Et}}\text{Im}][\text{Cl}]\text{ (1)}$, $[(3,3)\text{O}_{\text{Et}}\text{Im}][\text{Cl}]\text{ (2)}$ and $[(4,3)\text{O}_{\text{Et}}\text{Im}][\text{Cl}]\text{ (4)}$ phases (Table 1).

Novel ILCEs which are non-toxic, recyclable, and economical are synthesized and employed for an efficient extraction of ^{85}Sr . The new imidazolium ionic liquid-type crown ethers described here possess polyoxyethylene (POE) substituent groups. Their increased density should allow the imidazolium cores to adhere more tightly in order to maximize an interaction. ILCEs have been found to behave like a multifunctional compound which discriminates a metal cation according to its ring size. Also, the ILCEs are expected to be used for an extraction of

Table 1. Distribution of ^{85}Sr (Bq)

ILCE	Distribution of ^{85}Sr (Bq)		D
	Aqueous layer	ILCE layer	
$[(2,2)\text{O}_{\text{Et}}\text{Im}][\text{Cl}]\text{ (1)}$	390	No detection	0
$[(3,3)\text{O}_{\text{Et}}\text{Im}][\text{Cl}]\text{ (2)}$	323	No detection	0
$[(3,2)\text{O}_{\text{Et}}\text{Im}][\text{Cl}]\text{ (3)}$	17	356	21
$[(4,3)\text{O}_{\text{Et}}\text{Im}][\text{Cl}]\text{ (4)}$	369	No detection	0

other radionuclides or heavy metals. The ionic liquid-type crown ethers obtain their selectivity through their ability to fine-tune and reorganize their crown ether structure and the resulting properties of the crown by changing their ring size and rigidity, changing their number and type of donor atoms, appending ionizable groups, and modifying their lipophilicity.

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- $^1\text{H NMR}$ (CDCl_3) of **1a**: 3.56–3.58 (m, 4H, OCH_2), 3.64–3.78 (m, 8H, OCH_2), 3.78 (t, 4H, $J = 4.5 \text{ Hz}$, CH_2Cl). $^1\text{H NMR}$ (CDCl_3) of **3**: 3.48–4.01 (m, 20H), 4.61 (t, 8H, $J = 4.5 \text{ Hz}$), 6.91 (d, 4H, $J = 1.8 \text{ Hz}$), 7.41 (s, 2H).