Evaluating the Effect of Ammonium Ions on the Separation Efficiency of Two Adjacent Lanthanides

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Introduction

Stable isotopes
Mo-98, Te-130, Lu-176, Ho-165 etc.

Radioisotopes (RI)
Tc-99m, I-131, Lu-177, Ho-166 etc.

Medical Applications

beta radiation
: *treatment of cancer*

^{166}Ho
^{177}Lu

gamma radiation
: *imaging*

Radiotherapeutic properties

► Production method of carrier-free RI

- The "indirect" technique for producing carrier-free ^{166}Ho

  : $^{164}Dy(n, \gamma)^{165}Dy(n, \gamma)^{166}Dy \xrightarrow{\beta^-} {}^{166}Ho$

- The "indirect" technique for producing carrier-free ^{177}Lu

  : $^{176}Yb(n, \gamma)^{177}Yb \xrightarrow{\beta^-} {}^{177}Lu$

  Need to separate the target material

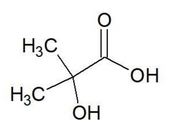
	57 La	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu
Ion radius (pm)	103	101	99.0	98.3	97.0	95.8	94.7	93.5	92.3	91.2	90.1	89.0	88.0	86.8	86.1

*Separation of two adjacent Ln has been achieved by ion-exchange chromatography with **cation-exchange resin** and **complexing agent**.*

► Ion-exchange Chromatography

Column separation setup
- Stationary phase
- Mobile phase (concentration, pH)
- Cation concentration

Separation consideration using α-HIBA



α-hydroxyisobutyric acid
(α-HIBA) pKa = 4.01

1. pH of the aqueous phase
   - acid-base equilibrium
2. Complex formation
   - Elution order: Lu-HIBA > Yb-HIBA
   - The smaller Lu^{3+} ion tend to form more stable complexes
3. **The interaction of the lanthanide with the functional groups of the stationary phase**

M. Van de Voorde *et al.* Coord. Chem. Rev. 382, 103 (2019)

Experiment and Results

► Separation of two adjacent lanthanides in Cold State
: Real-time evaluation technique

Two adjacent lanthanides are separated by a small difference in their binding stability constant with a complexing agent. In addition, it can be eluted by effectively displacing the lanthanide bound to the resin with any other cation such as NH_4^+.

$$n NH_4^+ + Ln^{3+}(R^-)_n \leftrightarrow Ln^{3+} + n(NH_4^+)(R^-)$$

The separation of Lu and Yb is investigated using primary, secondary and tertiary ammonium ions in addition to NH_4^+ ion. α-HIBA eluent adjusted to pH with methylamine, ethylamine, diethylamine, pyridine, ethanolamine, ethylenediamine.

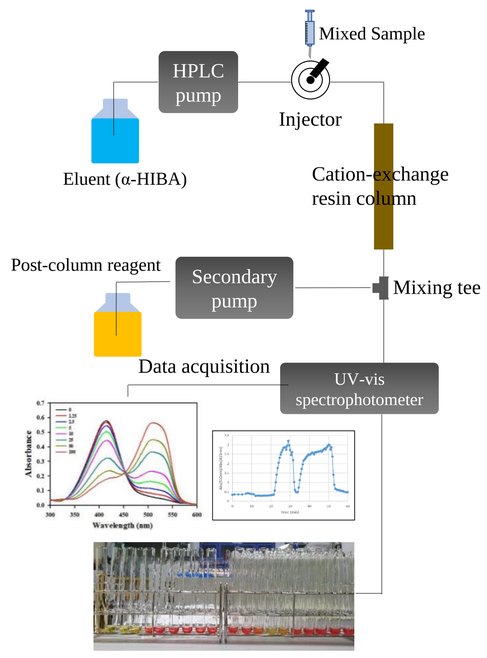
$$n CH_3NH_3^+ + Ln^{3+}(R^-)_n \leftrightarrow Ln^{3+} + n(CH_3NH_3^+)(R^-)$$

$Ln^{3+} = Lu^{3+}$ or Yb^{3+}
R = cation-exchange resin

HPLC instrument with post-column reaction system components

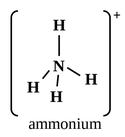
Separation of lanthanide ion onto the column was **confirmed by on-line monitoring** of the effluent using post-column derivatization reagent (chromogenic complexing reagent).

→ radioactive waste ↓
→ provides a variety of information including column reuse and reproducibility within a short time.

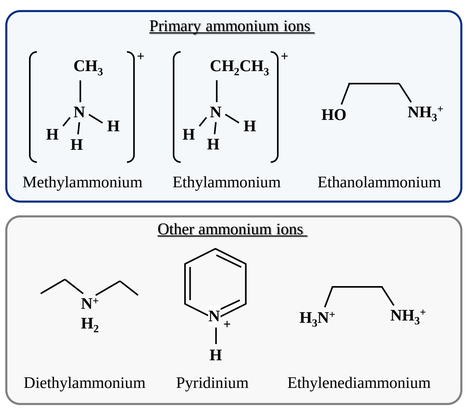


Sample fractions

The conjugate acids (protonated amines) of amines

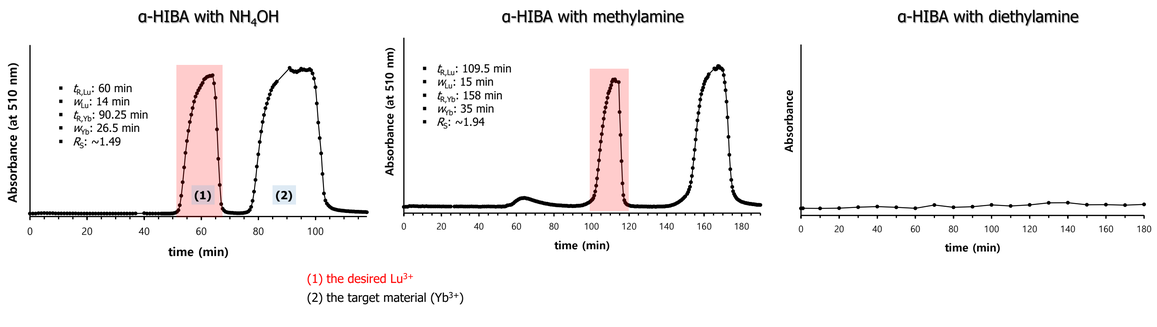


ammonium

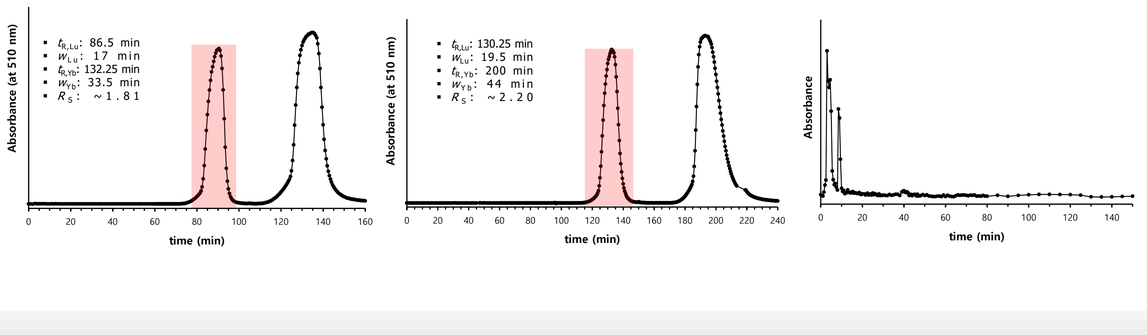


► Effects of the types of ammonium ion on the separation efficiency

Chromatogram of separation of Lu and Yb by α-HIBA with different amines

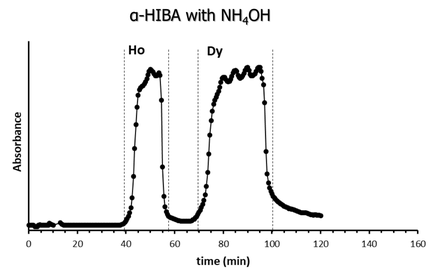


(1) the desired Lu^{3+}
(2) the target material (Yb^{3+})



- These results are due to changes in interaction and binding affinity between the eluent and the stationary phase.
- The higher the amine order, the longer the retention time and elution time.
- The use of secondary or higher amines could not observe the elution of Yb and Lu within 3 h.

Chromatogram of separation of Ho and Dy



Improvement of separation efficiency by changing ammonium ion

Conclusion

► In this study, the separation efficiency of two adjacent lanthanides (*eg.* Yb/Lu and Dy/Ho) was evaluated according to the types of ammonium ions such as primary, secondary and tertiary ammonium ions.

► It was found that the use of higher order amines results in longer column retention times and elution times.

► The selection of an appropriate the ammonium ion can effectively and selectively separate two adjacent lanthanides, as well as save the use of resin and eluent.