Solvent Extraction Research and Development, Japan, **Vol. 30, No 1, 59 – 69 (2023)**

Extraction of Metal Ions Using a Calix[4]arene Carboxylic Acid Derivative in Aromatic Ethers

Tatsuya OSHIMA[1],*, Tokiya ASANO[1], Tatsuya ISHIBASHI[1], Kaoru OHE[1],
Keisuke OHTO[2] and JUMINA[3]

[1]Department of Applied Chemistry, Faculty of Engineering, University of Miyazaki, 1-1 Gakuen Kibanadai-nishi, Miyazaki 889-2192, Japan; [2] Department of Chemistry and Applied Chemistry, Faculty of Science and Engineering, Saga University, 1-Honjo, Saga 840-8502, Japan; [3]Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Gadjah Mada, Yogyakarta, Indonesia

** Corresponding author: oshimat@cc.miyazaki-u.ac.jp*

(Received June 4, 2022; Accepted August 10, 2022)

If calixarenes can be dissolved in a relatively safe non-halogen solvent, they can be used in a liquid-liquid extraction process suitable for mass processing. In the present study, extraction behavior of metal ions using a calix[4]arene carboxylic acid derivative (^{t}Oct[4]CH_2COOH) dissolved in aromatic ethers was investigated. The solubility of ^{t}Oct[4]CH_2COOH in aromatic ethers decreases with increase of the length of aliphatic side chain of the ethers. The solubility of ^{t}Oct[4]CH_2COOH in 1-butoxybenzene (BB) was 28.0 mmol/L, which is smaller than that in chloroform but is higher than those in hexane and toluene. Divalent metal ions Mn(II), Co(II), Ni(II), Cu(II), Zn(II), and Pb(II) were extracted using ^{t}Oct[4]CH_2COOH in BB through proton exchange reaction at similar pH range in toluene, which is higher than that in chloroform. The extraction reaction of Cu(II) using ^{t}Oct[4]CH_2COOH in BB was determined by slope analysis and loading test. The stoichiometry between ^{t}Oct[4]CH_2COOH and Cu(II) was 2:1.

1. Introduction

Macrocyclic compounds calixarenes have been used as a platform to develop powerful extractants for various metal ions. The macrocyclic structure is favorable for the arrangement of multiple functional groups at the lower rims as well as the upper rims. Many kinds of calixarene derivatives which show excellent extractability and/or selectivity for targeted metal ions have been developed [1-3]. As calixarene derivatives have the inherent drawback in low solubility in hydrocarbons, studies on liquid-liquid extraction using calixarene derivatives generally have been conducted with chlorinated solvents such as chloroform and dichloromethane. However, the chlorinated solvents are hard to be used in industrial metal refining processes due to their high toxicity and high solubility in aqueous phase (e.g. 8.0 g/L for chloroform). Despite these drawbacks, most of the metal extraction studies using calixarene derivatives have been conducted using chlorinated solvents even in the last decades [4-8].

Two main approaches have been attempted to improve the solubility of calixarene derivatives. The first is to increase the solubility of calixarenes by introducing functional groups. The solubility of the calix[4]arene derivatives increases as the increase of alkyl chain length at rims [9]. Yamada and coworkers synthesized a series of higher-chain-length alkyl amino derivatives based on calix[4]arene for the improvement of the solubility in hydrocarbons [10]. Solubility of calixarene amino derivatives in hydrocarbons (toluene, xylene, kerosene, and Shellsol D70) increased with the increase of the length of alkyl chains. However, addition of 1-decanol as a phase modifier was necessary to suppress the formation of a third phase on the Pd(II) and Pt(IV) extraction. The mixed alkylated calix[4]arene tetraacetic acid derivatives were also prepared, because break of symmetry of calix[4]arene by introducing different alkyl chains is also effective for the improvement of the solubility [11]. However, pure synthesis of the asymmetric calixarene derivatives is not easy. Dissolution of calixarene derivatives into various types of media has also been attempted as the second approach. Extraction of metal ions using *p-tert*-butylcalixa[4]arene carboxylate derivative dissolved in isooctane using reversed micelles was reported [12]. Ionic liquids are also used as solvents for calixarene derivatives [13-15]. For instance, extraction of Cs(I) using 1,3-[(2,4-diethylheptylethoxy)oxy]- 2,4-crown-6-calix[4]arene in an ionic liquid was recently reported [16]. However, existing ionic liquids are difficult to use as solvents industrially due to their high viscosity and cost. Adsorption of metal ions using adsorbents incorporating calixarene derivatives is another strategy for utilizing the host compounds without dissolution into organic solvents [17]. Methods of metal adsorption using calixarene derivatives can be classified into four types; polymer-supported adsorbents, impregnated adsorbents (and polymer inclusion membranes), crosslinked adsorbents, and polymerized adsorbents (vinyl polymerization and copolymerization without vinyl polymerization) [18]. However, the adsorption process is inferior to liquid-liquid extraction in terms of mass processing of metals. For large-scale metal refining using calixarene derivatives, development of solvents that shows low toxicity and has good physical characteristics for industrial operations is required.

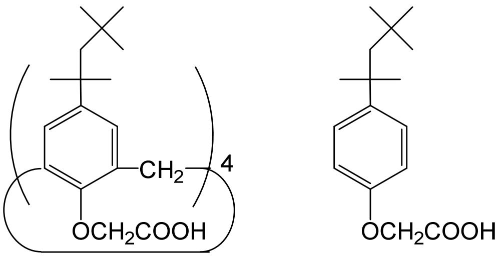
The present study focuses on dissolution of a calix[4]arene carboxylic acid derivative. *p-tert*-Octylcalix[4]arene tetracarboxylic acid derivative (abbreviated as ^{t}Oct[4]CH_2COOH) has appeared as an excellent extractant for various metal ions. In early studies, ^{t}Oct[4]CH_2COOH has been developed as an extractant for rare earth metal ions [19-21]. Sodium ion is selectively extracted using ^{t}Oct[4]CH_2COOH from other alkali metal ions, while divalent alkali earth and transition metal ions are also extracted [22]. Trivalent metal ions Fe(III), In(III), and Ga(III) can be extracted selectively over Zn(II) [23]. Moreover, extractability of ^{t}Oct[4]CH_2COOH for metal ions is enhanced by the allosteric coextraction of Na(I), resulting in the extraction of metal ions under lower pH condition [20,24-26]. Whereas typical calix[4]arene derivatives bear tert-butyl groups, ^{t}Oct[4]CH_2COOH bears plural *tert*-octyl groups at the upper rims, which contribute to improved solubility in organic solvents. The solubilities of ^{t}Oct[4]CH_2COOH in chloroform, toluene, and hexane are higher than those of *p-tert*-butyl and *p-tert*-amylcalixa[4]arene tetraacetic acid derivatives [9]. Nonetheless, the solubilities of ^{t}Oct[4]CH_2COOH in hydrocarbons such as hexane and toluene are less than 20 mmol/L and are insufficient for industrial mass processing.

In the present study, aromatic ethers were assessed as solvents for ^{t}Oct[4]CH_2COOH to develop liquid-liquid extraction system for metal ions. Aromatic ethers are expected as good solvents for calixarene derivatives due to their structural similarity. Solubility of ^{t}Oct[4]CH_2COOH in aromatic monoethers methoxybenzene (anisole, MB), 1-butoxybenzene (BB), and 1-octoxybenzene (OB) were compared with those in typical hydrocarbons. Subsequently, extraction behaviors for divalent transition metal ions using ^{t}Oct[4]CH_2COOH in BB and chloroform were investigated to compare the extractability, selectivity for metal ions, and the extraction mechanism in the solvents. Recently, the authors studied extraction of amino acid esters and a protein using *p-tert*-octylcalix[6]arene carboxylic acid derivative (^{t}Oct[6]CH$_2$COOH) in the aromatic ethers [27]. The solubilities of ^{t}Oct[6]CH$_2$COOH in BB and MB were more than 20 mmol/L. Tryptophan methyl ester and a cationic protein cytochrome *c* were extracted ^{t}Oct[6]CH$_2$COOH in BB. Similarly, extraction system for metal ions using ^{t}Oct[4]CH$_2$COOH was expected to be constructed using the aromatic ethers as solvents.

2. Experimental

2.1 Reagents

Figure 1 shows the molecular structures of ^{t}Oct[4]CH$_2$COOH and *p-tert*-octylphenoxyacetic acid (abbreviated as ^{t}Oct[1]CH$_2$COOH, as the monomer analog). ^{t}Oct[4]CH$_2$COOH and ^{t}Oct[1]CH$_2$COOH were synthesized according to the procedures shown in a previous paper [19]. ^{t}Oct[4]CH$_2$COOH was synthesized as cone conformation. The final product was purified by recrystallization and identified by ^{1}H-NMR. OB and BB (Figure 2) were synthesized according to the procedures shown in previous papers [28,29]. However, the purification step by washing was conducted with greater care [30]. The final products were identified by ^{1}H-NMR. Analytical-grade manganese(II), cobalt(II), nickel(II), copper(II), zinc(II), and lead(II) chlorides were purchased from FUJIFILM Wako Pure Chemical Corporation (Osaka, Japan) and used without further purification for the metal ion solutions. Analytical grade MB was purchased from Tokyo Kasei Co. Ltd, (Tokyo, Japan). All other reagents were reagent grade and were used as received.



^{t}Oct[4]CH$_2$COOH (cone conformation) ^{t}Oct[1]CH$_2$COOH

Figure 1. Structures of ^{t}Oct[n]CH$_2$COOH (n = 1,4).

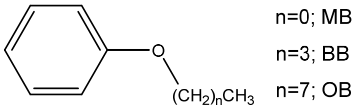


Figure 2. Structures of MB, BB, and OB.

2.2 Property of solvents

Saturated solubility of ^{t}Oct[4]CH$_2$COOH in each solvent was determined as follows. Excess ^{t}Oct[4]CH$_2$COOH was added to each solvent (aromatic ethers in Figure 2, hexane, isooctane, dodecane, or toluene) so that the solute remained undissolved. After filtration of the undissolved ^{t}Oct[4]CH$_2$COOH using Kiriyama No. 5C filter paper (Kiriyama Glass Works Co., Tokyo, Japan), the filtrate (5.00 mL) was dried *in vacuo* to recover dissolved ^{t}Oct[4]CH$_2$COOH. Dry mass of ^{t}Oct[4]CH$_2$COOH in the filtrate was weighted an electronic balance (Sartorius CP225D, Goettingen, Germany) to determine the solubility. Other physical properties are cited from the values investigated in a previous study [27].

2.3 Extraction of metal ions using ^{t}Oct[4]CH$_2$COOH

Liquid-liquid extraction tests for metal ions using ^{t}Oct[4]CH$_2$COOH were conducted batch-wise as follows. An aqueous solution containing a 0.10 mmol/L Mn(II), Co(II), Ni(II), Cu(II), Zn(II), and Pb(II) was prepared. The pH of the aqueous solution was adjusted using 100 mmol/L HEPES (4-(2-hydroxyethyl)-1-

piperazineethanesulfonic acid) buffer and a small quantity of hydrochloric acid or lithium hydroxide. As the size of lithium ion is much smaller compared with the cavity size of ^{t}Oct[4]CH_2COOH, lithium ion should not be extracted by ^{t}Oct[4]CH_2COOH and not influence the extraction of divalent metal ions [22]. An organic solution was prepared by dissolving 10 mmol/L ^{t}Oct[4]CH_2COOH or 40 mmol/L ^{t}Oct[1]CH_2COOH in a solvent (BB, toluene, or chloroform). The organic solution (1.0 mL) and the aqueous solution (5.0 mL) were mixed in a screw capped glass vial; the volume ratio between organic phase and the aqueous phase is at 1:5 (O/A = 0.2). The mixture was shaken (120 rpm) in a thermostatted water bath at 30 °C. After 24 h, each phase was separated and the equilibrium pH was measured. The initial and equilibrium concentrations of metal ions in the aqueous phases were determined using an atomic absorption spectrophotometer (Shimadzu AA-7000, Shimadzu Co., Kyoto, Japan). As the volume of aqueous and organic phase was same before and after extraction, the extraction percentage and distribution ratio (*D*) of the metal were calculated according to Equations (1) and (2), respectively [19,25,27];

$$\mathit{Extraction}\,[\%] = \frac{[\mathrm{M}]_{\mathrm{aq,init}} - [\mathrm{M}]_{\mathrm{aq,eq}}}{[\mathrm{M}]_{\mathrm{aq,init}}} \times 100 \tag{1}$$

$$D = \frac{[\mathrm{M}]_{\mathrm{org,eq}}}{[\mathrm{M}]_{\mathrm{aq,eq}}} = \frac{5 \times \left([\mathrm{M}]_{\mathrm{aq,init}} - [\mathrm{M}]_{\mathrm{aq,eq}}\right)}{[\mathrm{M}]_{\mathrm{aq,eq}}} \tag{2}$$

where $[\mathrm{M}]_{\mathrm{aq,init}}$ represents the initial concentration of metal ions in the aqueous phase, and $[\mathrm{M}]_{\mathrm{aq,eq}}$ and $[\mathrm{M}]_{\mathrm{org,eq}}$ are the total concentrations of metal ions in the aqueous and organic phases, respectively, at equilibrium. As the concentration of metal ion is concentrated 5 times in the organic phase (O/A = 0.2), the decrease of metal concentration in the aqueous solution is multiplied 5 times in eq. (2).

Additionally, extraction of Cu(II) using ^{t}Oct[4]CH_2COOH was conducted by contacting an aqueous solution (5.0 mL) containing 0.10 – 4.0 mmol/L Cu(II) and 100 mmol/L HEPES with BB solution containing extractant (1.0 mL) to investigate stoichiometry of the complex. The loading percentage of Cu(II) to ^{t}Oct[4]CH_2COOH was calculated by using eq. (3):

$$\mathit{Loading}\,[\%] = \frac{[\mathrm{Cu(II)}]_{\mathrm{org,eq}}}{[{}^{t}\mathrm{Oct[4]CH_2COOH}]_{\mathrm{org,init}}} \times 100 = \frac{5 \times \left([\mathrm{Cu(II)}]_{\mathrm{aq,init}} - [\mathrm{Cu(II)}]_{\mathrm{aq,eq}}\right)}{[{}^{t}\mathrm{Oct[4]CH_2COOH}]_{\mathrm{org,init}}} \times 100 \tag{3}$$

where $[{}^{t}\mathrm{Oct[4]CH_2COOH}]_{\mathrm{org,init}}$ represents the initial concentration of ^{t}Oct[4]CH_2COOH in the organic phase.

2.4 Back extraction of Cu(II)

The forward extraction of 0.10 mmol/L Cu(II) using 10 mmol/L ^{t}Oct[4]CH_2COOH in chloroform and BB was performed from the aqueous to the organic phase (2.0 mL/10.0 mL, O/A = 0.2) in a similar manner to that shown in the above section. The organic phase containing Cu(II) (1.5 mL) was contacted with a 1.5 mL fresh aqueous solution containing a different mineral acid. Both phases were mixed and shaken at 30˚C for 24 h. The stripping solution was separated from the organic phase and the back extraction percentage (*B.E.* [%]) was calculated according to eq. (4).

$$\mathit{B.E.}[\%] = \frac{[\mathrm{Cu(II)}]_{\mathrm{aq,eq}}}{[\mathrm{Cu(II)}]_{\mathrm{org,init}}} \times 100 \tag{4}$$

where $[\mathrm{Cu(II)}]_{\mathrm{org,init}}$ represents the initial concentration of the metal ion in the organic phase and $[\mathrm{Cu(II)}]_{\mathrm{aq,eq}}$ is the total concentration of the metal ion in the aqueous phase after back extraction.

3. Results and Discussion

3.1 Solubility of ^{t}Oct[4]CH$_2$COOH in aromatic ethers

In liquid-liquid extraction system, organic solvents which are used as diluents of extractants must not only exhibit high solubility, but also meet physical properties required in industrial processes. Table 1 summarizes properties of aromatic ethers and other solvents. The solubility of ^{t}Oct[4]CH$_2$COOH in aliphatic hydrocarbons is quite low. The solubility in chloroform is the highest in Table 1. The solubility of ^{t}Oct[4]CH$_2$COOH in the aromatic ethers decreases with increase of the length of aliphatic side chain; 49.8 mmol/L in MB, 28.0 mmol/L in BB, and 12.8 mmol/L in OB. It should be noted that the solubility in aromatic ethers MB and BB is next to that in chloroform and higher than that in toluene. On the other hand, the solubility of the solvents in water should be low to minimize leak of the solvent into the aqueous phase. Chloroform is a good solvent for various calixarene derivatives but is not suitable for industrial solvent extraction processes due to its toxicity and leakage into water. The aqueous solubility of MB is also relatively high. The aqueous solubilities of BB and OB are much smaller than those of chloroform, MB, and toluene. A high flash point is also an important requirement for the solvent in view of safe operation. The flash point of MB (51.7 °C) is higher than those of hexane and toluene. From the relatively high boiling points of BB and OB, the flash points of BB and OB are expected to be higher than MB. The relatively high viscosity of OB (3.29 mPa·s) is not desirable for easy operation of the solvent extraction process. Moreover, the densities of aromatic ethers including BB are close to that of water, which is undesirable from the viewpoint of phase separation. Comprehensive consideration of the solubility of calixarene and the above physical properties, BB was evaluated as a solvent for ^{t}Oct[4]CH$_2$COOH in the following experiments.

Table 1. Properties of aromatic ethers and other solvents.

solvent	molar mass [g mol^{-1}]	density [g/L]	viscosity [mPa·s]	boiling point ^{a} [°C]	flash point [°C]	logP ^{b} [-]	solubility in water [g/L]	solubility of ^{t}Oct[4]CH$_2$COOH [mmol/L]
MB	108.1	0.996	1.01	154	51.7	2.11	1.52	49.8
BB	150.2	0.956	1.79	204 ^{a}	–	3.14	3.9×10^{-3}	28.0
OB	206.3	0.916	3.29	296 ^{a}	–	4.92	$< 2 \times 10^{-3}$	12.8
chloroform	119.4	1.48	0.53	61	nonflammable	1.97	8.0	63.0^{c}
hexane	86.2	0.66	0.31	69	–22	3.30	9.5×10^{-3}	0.54
isooctane	114.2	0.69	0.63	116	9.9	3.62	5.6×10^{-4}	< 0.006
dodecane	170.3	0.75	1.38	216	74	6.12	1.8×10^{-4}	< 0.06
Exxsol D80	mixture	0.82	1.77	210	91	mixture	–	< 0.054^{c}
toluene	92.1	0.867	0.59	111	4	2.73	0.47	19.1

– not measured; a estimated by using *ChemDraw* ver. 19.0 (PerkinElmer, Inc., MA, USA); b estimated by using *MarvinSketch 6.2.1* software (ChemAxon Ltd., Budapest, Hungary) and the KLOP method [31]; c cited from Ref. [9]

3.2 Extraction of divalent metal ions using ^{t}Oct[4]CH$_2$COOH in aromatic ether

In previous studies, high performance of ^{t}Oct[4]CH$_2$COOH as an acidic extractant for various metal cations in toluene and chloroform has been reported [9,19-22]. As a preliminary test to investigate the extraction behavior of ^{t}Oct[4]CH$_2$COOH in aromatic ethers, extraction of Cu(II) using Oct[4]CH$_2$COOH and the monomer analog ^{t}Oct[1]CH$_2$COOH in BB was compared with that in toluene and chloroform (Figure 3). Cu(II) was not extracted at all just contacting with organic solvents without extractants. The initial concentration of ^{t}Oct[4]CH$_2$COOH was 10 mmol/L, while the concentration of ^{t}Oct[1]CH$_2$COOH was 40 mmol/L to adjust the number of functional carboxyl groups to that of ^{t}Oct[4]CH$_2$COOH. As the extraction of metal ions using acidic extractants is based on a proton exchange reaction, the extraction increases with increasing pH. Cu(II) was extracted using the monomer analog ^{t}Oct[1]CH$_2$COOH at pH more than 4. The extractability of ^{t}Oct[1]CH$_2$COOH for Cu(II) is higher than that of a commercial carboxylic acid extractant Versatic 10 due to the higher acid dissociation constant [32]. The extractability of the macrocyclic compound ^{t}Oct[4]CH$_2$COOH is higher than that of ^{t}Oct[1]CH$_2$COOH due to the chelating effect [22]. The pH value for 50 % extraction (pH$_{1/2}$) of Cu(II) using ^{t}Oct[4]CH$_2$COOH in BB was 2.87, which is much smaller than that using ^{t}Oct[1]CH$_2$COOH (4.44). It should be noted that the pH region for the extraction using ^{t}Oct[4]CH$_2$COOH in BB is almost similar to that in chloroform, which are slightly lower than that in toluene. The result suggests that the stability of the complex between Cu(II) and ^{t}Oct[4]CH$_2$COOH in BB is similar to that in chloroform.

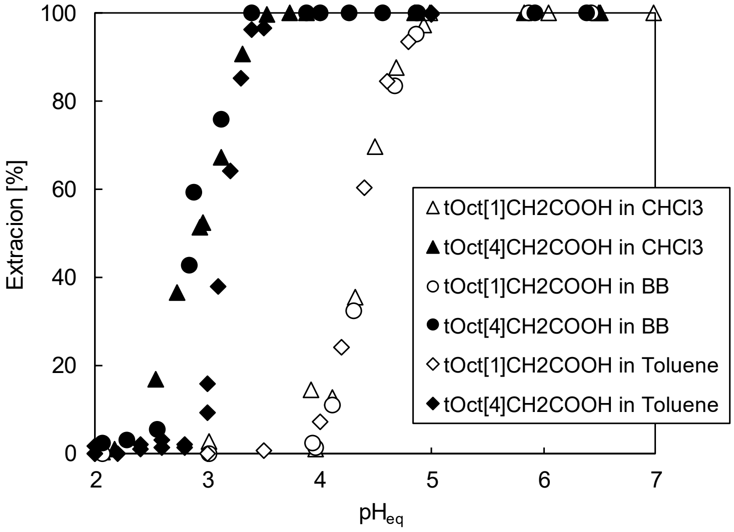


Figure 3. Extraction of Cu(II) using ^{t}Oct[*n*]CH$_2$COOH (*n*=1,4) in various solvents as a function of equilibrium pH: O/A = 0.2, [Cu(II)]$_{init}$ = 0.1 mmol/L, [^{t}Oct[4]CH$_2$COOH]= 10.0 mmol/L.

Figure 4 shows the extraction of divalent metal ions using ^{t}Oct[4]CH$_2$COOH in chloroform (a) and in BB (b). The order of the extraction in chloroform is Pb(II) > Cu(II) > Mn(II) > Ni(II), Zn(II) > Co(II), which roughly agrees with that using carboxylic acid extractants except for Mn(II) [22,33]. In particular, ^{t}Oct[4]CH$_2$COOH shows strong affinity to Pb(II) due to the accurate three-dimensional arrangement of coordinating oxygen atoms [3,9]. In a previous study, coordination of tetrameric phenoxy and oxygens and carbonyl oxygens for the complexation between Pb(II) and ^{t}Oct[4]CH$_2$COOH was suggested by ^{1}H-NMR spectra [34]. The order of the extraction in BB is Pb(II) > Cu(II) > Mn(II), Ni(II), Zn(II), Co(II), which is similar to that in chloroform, except for the extraction of Mn(II) was slightly decreased. From the result in Figure 4(b), the extraction process for Pb(II) and Cu(II) using ^{t}Oct[4]CH$_2$COOH in BB can be constructed. In contrast, Mn(II), Ni(II), Zn(II), and Co(II) cannot be separated mutually using ^{t}Oct[4]CH$_2$COOH in BB.

Table 2 summarizes pH$_{1/2}$ values of for the extraction of divalent metal ions using ^{t}Oct[4]CH$_2$COOH in chloroform and in BB. Most of the pH$_{1/2}$ values for each metal ion in BB are similar to those in chloroform except for Mn(II). The reason of the different extraction profiles for Mn(II) in Figures 4(a) and (b) is not clear.

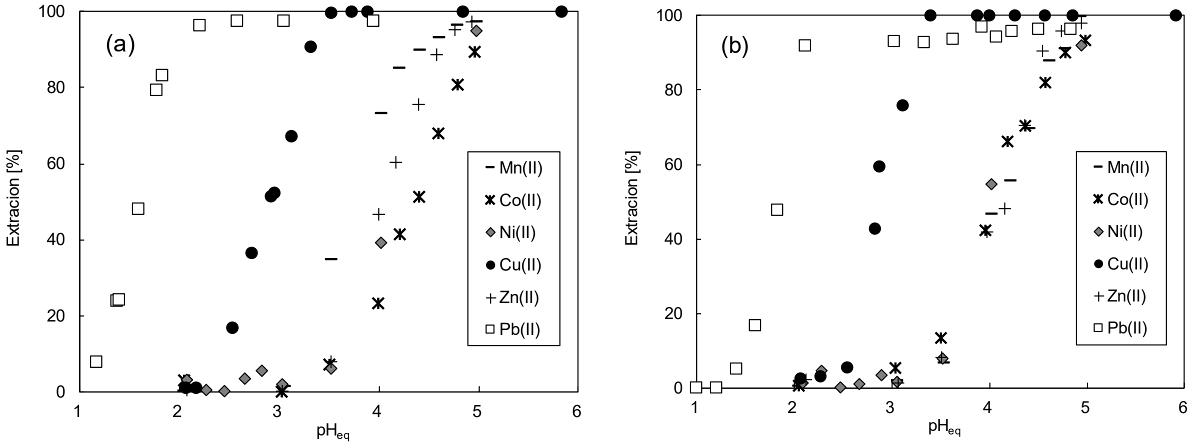


Figure 4. Extraction profiles of divalent metal ions using ^{t}Oct[4]CH$_2$COOH in chloroform (a) and in BB (b): O/A = 0.2, [metal ion]$_{init}$ = 0.1 mmol/L, [^{t}Oct[4]CH$_2$COOH]= 10.0 mmol/L.

Table 2. The pH$_{1/2}$ values of for the extraction of divalent metal ions using ^{t}Oct[4]CH$_2$COOH in chloroform and in BB.

solvent	pH$_{1/2}$					
	Mn(II)	Co(II)	Ni(II)	Cu(II)	Zn(II)	Pb(II)
chloroform	3.24	4.34	4.20	2.90	4.09	1.58
BB	4.16	4.07	4.15	2.91	4.10	1.81

3.3 Determination of extraction reaction in BB

The extraction reaction for Cu(II) using ^{t}Oct[4]CH$_2$COOH in BB was investigated with slope analysis and loading test.

The effect of the equilibrium pH on the distribution ratio of Cu(II) is shown in Figure 5. The slope of the line obtained by plotting the logarithm of the distribution ratio of Cu(II) and the equilibrium pH was 2, which indicates that two hydrogen ions are released from ^{t}Oct[4]CH$_2$COOH molecules for the extraction of Cu(II). The effect of ^{t}Oct[4]CH$_2$COOH concentration on the distribution ratio of Cu(II) is shown in Figure 6. The logarithm of the distribution ratio increased with increasing concentration of ^{t}Oct[4]CH$_2$COOH. The slope of the line obtained by plotting the logarithm of the distribution ratio of Cu(II) against the logarithm of the ^{t}Oct[4]CH$_2$COOH concentration in BB was 2.

Figure 7 shows the loading profile of Cu(II) to ^{t}Oct[4]CH$_2$COOH in BB as a function of initial Cu(II) concentration. The molar ratio of the extracted Cu(II) to ^{t}Oct[4]CH$_2$COOH increases with the increase of initial concentration of Cu(II) and approaches the constant value 0.5. The result suggests that the stoichiometry between Cu(II) and ^{t}Oct[4]CH$_2$COOH is 1 : 2.

Based on the results in Figures 5, 6, and 7, the extraction reaction of Cu(II) using ^{t}Oct[4]CH$_2$COOH in BB can be represented as

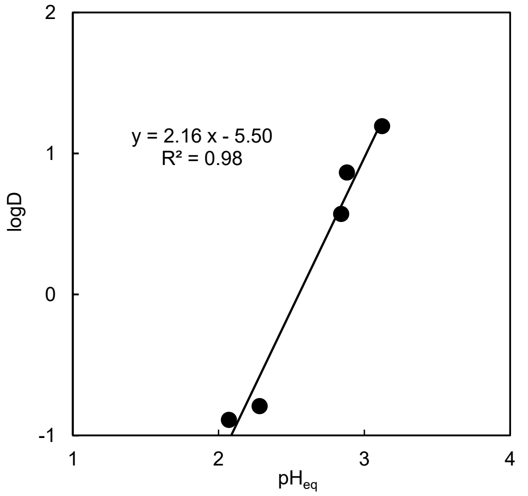


Figure 5. Effect of the equilibrium pH on the distribution ratio of Cu(II): O/A = 0.2, pH$_{eq}$ 2.07-3.32, [^{t}Oct[4]CH$_2$COOH] = 10.0 mmol/L, [Cu(II)]$_{init}$ = 0.1 mmol/L.

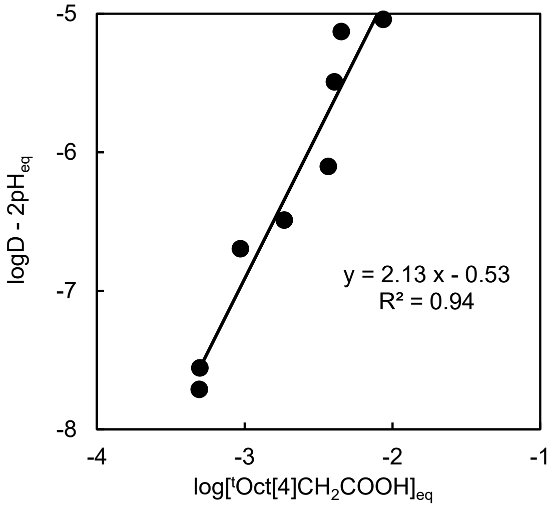


Figure 6. Effect of the concentration of ^{t}Oct[4]CH$_2$COOH on the distribution ratio of Cu(II): O/A = 0.2, pH$_{eq}$ 2.90-3.00, [^{t}Oct[4]CH$_2$COOH]=0.5 – 10.0 mmol/L, [Cu(II)]$_{init}$ = 0.1 mmol/L.

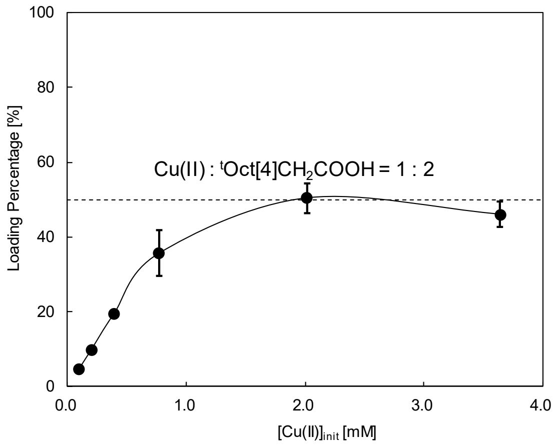


Figure 7. The loading profile of Cu(II) to ^{t}Oct[4]CH$_2$COOH in BB as a function of initial Cu(II) concentration.

$$\mathrm{Cu^{2+}} + 2\overline{\mathrm{H_4R}} = \overline{\mathrm{Cu^{2+}(H_3R^-)_2}} + 2\mathrm{H^+} \qquad (5)$$

The bar denotes species in the organic phase, and H$_4$R denotes ^{t}Oct[4]CH$_2$COOH. Two ^{t}Oct[4]CH$_2$COOH molecules form complex with Cu(II) and neutralize charges by proton exchange reaction.

In case of analysis based on eq. (5), the extraction equilibrium constant for Cu(II) $K_{\mathrm{Cu(II)}}$ is given by eq. (6):

$$K_{\mathrm{Cu(II)}} = \frac{\overline{[\mathrm{Cu^{2+}(H_3R^-)_2}]}[\mathrm{H^+}]^2}{[\mathrm{Cu^{2+}}][\overline{\mathrm{H_4R}}]^2} \qquad (6)$$

and the distribution ratio of Cu(II) between the organic and aqueous phases is defined by eq. (7):

$$D = \frac{[\mathrm{Cu(II)}]_{org,eq}}{[\mathrm{Cu(II)}]_{aq,eq}} = \frac{\overline{[\mathrm{Cu^{2+}(H_3R^-)_2}]}}{[\mathrm{Cu^{2+}}]} \qquad (7)$$

By combining eqs. (6) and (7), eq. (8) in its logarithmic form can be obtained:

$$\log D = 2\mathrm{pH} + 2\log[\overline{\mathrm{H_4R}}] + \log K_{\mathrm{Cu(II)}} \qquad (8)$$

According to eq. (8), the experimental log D data in BB based on the results in Figures 5 and 6 are plotted in Figure 8. For the results in BB (Figure 8 (a)), the plots from pH dependency (Figure 5) and those from

^{t}Oct[4]CH$_2$COOH concentration dependency (Figure 6) were almost on the same straight line, suggesting that eq. (8) is suitable for the extraction in BB. The extraction equilibrium constants ($K_{\mathrm{Cu(II)}}$) in BB was evaluated from the intercept of the theoretical straight line with the ordinate of Figure 8 (a) as 4.14 × 10^{-2} [–].

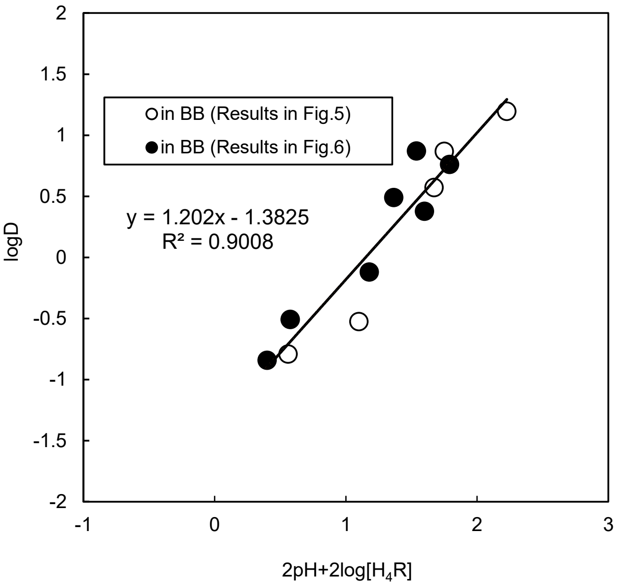


Figure 8. Logarithmic distribution ratio of Cu(II) using ^{t}Oct[4]CH$_2$COOH as a function of pH and the concentration of ^{t}Oct[4]CH$_2$COOH in BB. The solid line is the theoretical line.

3.4 Back extraction

As the extraction of Cu(II) using ^{t}Oct[4]CH$_2$COOH proceeds by proton exchange reaction, the extracted Cu(II) should be recovered by contacting an aqueous acidic solution. Table 3 summarizes the back-extraction percentage of Cu(II) using mineral acids. In chloroform system, Cu(II) was effectively stripped from the organic phase by contacting 0.1–1.0 mol/L HCl, expect for the decrease of stripping in 3.0 mol/L HCl. In contrast, back extraction of Cu(II) by mineral acid from BB was inefficient: Back extraction increases with the increase of HCl concentration, however, back extraction was 62.4 % even using 3.0 mol/L HCl. Vortex and prolonged shaking were also ineffective for back extraction of Cu(II) from BB. The low back extraction of Cu(II) from BB is strange, because the forward extraction profile of Cu(II) in BB is similar to that in chloroform (Figure 3). BB might influence the stability of the complex between Cu(II) and ^{t}Oct[4]CH$_2$COOH and/or the reverse reaction, but further research is necessary to clarify the mechanism.

Table 3. Back extraction of Cu(II) extracted using ^{t}Oct[4]CH$_2$COOH. O/A = 1.0, [Cu(II)]$_{\mathrm{init}}$ = 0.1 mmol/L, [^{t}Oct[4]CH$_2$COOH] = 10 mmol/L.

Back-extraction reagent	Stripping [%]	
	in chloroform	in BB
0.01 mol/L HCl	30.6	0.0
0.1 mol/L HCl	100.0	5.2
0.5 mol/L HCl	99.1	19.2
1.0 mol/L HCl	96.6	21.5
3.0 mol/L HCl	57.0	62.4
0.1 mol/L HNO$_3$	97.4	17.8
0.05 mol/L H$_2$SO$_4$	83.9	1.0

4. Conclusion

In the present study, aromatic ethers are assessed as solvents for calixarene derivatives to construct solvent extraction processes for metal ions. The solubility of ^{t}Oct[4]CH$_2$COOH increased as the alkyl chain length of aromatic ethers is shorter. BB is likely a best solvent in the series of aromatic ethers in views of solubility of ^{t}Oct[4]CH_2COOH, less aqueous solubility, and expected high flash point. Divalent metal ions such as Pb(II) and Cu(II) were extracted using ^{t}Oct[4]CH_2COOH dissolved in BB. As the extraction behavior of metal ions in BB is similar to that in chloroform, BB would be an alternative solvent for ^{t}Oct[4]CH_2COOH. However, further research is necessary to establish back-extraction conditions for metal ions. Since calixarene was appeared as a new host compound, a number of extraction processes for metal ions using calixarene derivatives has been developed. However, they have hardly been put into practical use so far. Safe solvents with high solubility can facilitate the practical application of the extraction process using calixarenes. From the results in this study, aromatic ethers are ones of the potential solvents for this goal.

Acknowledgement

This research was supported by the Adaptable and Seamless Technology Transfer Program through Target-driven R&D (A-STEP, VP30118067391), of the Japan Science and Technology Agency (JST), Japan.

References

1) V. Böhmer, *Angew. Chem., Int. Ed.*, **34**, 713-745 (1995).
2) R. Ludwig, *Fresenius' J. Anal. Chem.*, **367**, 103-128 (2000).
3) K. Ohto, '*Molecular design and metal extraction behavior of calixarene compounds as host extractants*' in "*Ion Exchange and Solvent Extraction: Volume 21, Supramolecular Aspects of Solvent Extraction*", ed. by B. A. Moyer, CRC Press, pp. 81-127 (2013).
4) S. Alpaydin, A. Ö. Saf, S. Bozkurt, A. Sirit, *Desalination*, **275**, 166-171 (2011).
5) Y. Yang, X. Cao, D. W. Purkiss, J. F. Cannon, R. A. Bartsch, *Tetrahedron*, **68**, 2233-2244 (2012).
6) J. P. Ward, J. M. White, C. G. Young, *Tetrahedron*, **69**, 8824-8830 (2013).
7) A. B. Chetry, T. Matsufuji, B. B. Adhikari, S. Morisada, H. Kawakita, K. Ohto, T. Oshima, Jumina, *J. Inclusion Phenom. Macrocyclic Chem.*, **81**, 301-310 (2015).
8) F.-Z. Xiao, Y.-Q. Pu, C. Wang, Y.-L. Xu, K. Zhang, C.-H. Ho,·G.-W. Peng,·S.-Y. He, *J. Radioanal. Nucl. Chem.*, **321**, 49-55 (2019).
9) K. Ohto, *Solvent Extr. Res. Dev., Jpn.*, **17**, 1-18 (2010).
10) M. Yamada, Y. Kaneta, M. R. Gandhi, U. M. R. Kunda, A. Shibayama, *Hydrometallurgy*, **184**, 103–108 (2019).
11) K. Ohto, H. Tanaka, H. Ishibashi, K. Inoue, *Solvent Extr. Ion Exch.*, **17**, 1309-1325 (1999).
12) F. Kubota, K. Shinohara, K. Shimojo, T. Oshima, M. Goto, S. Furusaki, T. Hano, *Sep. Purif. Technol.*, **24**, 93-100 (2001).
13) H. Luo, S. Dai, P. V. Bonnesen, A. C. Buchanan III, J. D. Holbrey, N. J. Bridges, R. D. Rogers, *Anal. Chem.*, **76**, 3078-3083 (2004).
14) K. Shimojo, M. Goto, *Anal. Chem.*, **76**, 5039-5044 (2004).
15) F. Kubota, M. Goto, *Solvent Extr. Res. Dev., Jpn.*, **13**, 23-36 (2006).
16) T. Takahashi, T. Ito, S.-Y. Kim, *J. Radioanal. Nucl. Chem.*, **316**, 1067-1073 (2018).
17) R. Zadmard, F. Hokmabadi, M. R. Jalali, A. Akbarzadeh, *RSC Adv.*, **10**, 32690-32722 (2020).
18) K. Ohto, *J. Inclusion Phenom. Macrocyclic Chem.*, **101**, 175-194 (2021).

19) K. Ohto, M. Yano, K. Inoue, T. Yamamoto, M. Goto, F. Nakashio, S. Shinkai, T. Nagasaki, *Anal. Sci.*, **11**, 893-902 (1995).

20) K. Ohto, M. Yano, K. Inoue, T. Nagasaki, M. Goto, F. Nakashio, S. Shinkai, *Polyhedron*, **16**, 1655-1661 (1997).

21) T. Kakoi, T. Nishiyori, T. Oshima, F. Kubota, M. Goto, S. Shinkai, F. Nakashio, *J. Membr. Sci.*, **136**, 261-271 (1997).

22) T. Kakoi, T. Toh, F. Kubota, M. Goto, S. Shinkai, F. Nakashio, *Anal. Sci.*, **14**, 501-506 (1998).

23) B. B. Adhikari, M. Gurung, H. Kawakita, K. Ohto, *Analyst*, **136**, 4570-4579 (2011).

24) K. Ohto, K. Shiratsuchi, K. Inoue, M. Goto, F. Nakashio, S. Shinkai, T. Nagasaki, *Solvent Extr. Ion Exch.*, **14**, 459-478 (1996).

25) T. Oshima, T. Kakoi, F. Kubota, K. Ohto, M. Goto, F. Nakashio, *Sep. Sci. Technol.*, **33**, 1905-1917 (1998).

26) K. Ohto, H. Ishibashi, H. Kawakita, K. Inoue, T. Oshima, *J. Inclusion Phenom. Macrocyclic Chem.*, **65**, 111-120 (2009).

27) T. Oshima, T. Asano, A. Inada, K. Ohto, Jumina, *J. Inclusion Phenom. Macrocyclic Chem.*, **102**, 507–514 (2022).

28) T. Horiuchi, T. Oshima, Y. Baba, *Hydrometallurgy*, **178**, 176-180 (2018).

29) T. Oshima, T. Horiuchi, K. Matsuzaki, K. Ohe, *Hydrometallurgy*, **183**, 207-212 (2019).

30) T. Oshima, K. Matsuzaki, A. Inada, K. Ohe, *Sep. Purif. Technol.*, **258**, 118008 (7 pages) (2021).

31) G. Klopman, J.-Y. Li, S. Wang, M. Dimayuga, *J. Chem. Inf. Comput. Sci.*, **34**, 752-781 (1994).

32) C. Kai, T. Oshima, Y. Baba, *Solvent Extr. Res. Dev., Jpn.*, **17**, 175-185 (2010).

33) L. Gotfryd, G. Pietek, Z. Szołomicki, K. Becker, J. Piwowońska, *Physicochem. Probl. Miner. Process.*, **51**, 435-445 (2015).

34) K. Ohto, Y. Fujimoto, K. Inoue, *Anal. Chim. Acta*, **387**, 61-69 (1999).