Design and Synthesis of the New Chelating Agent and Its Extraction Behavior of Soft Metal Ion

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Design and Synthesis of the New Chelating Agent and Its Extraction Behavior of Soft Metal Ion

(新規キレート配位子の創製およびソフト金属抽出機能評価)

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Abbrebiations

Ac	acetyl
AIBN	2,2'-azobis(isobutyronitrile)
aq.	aqueous solution
Ar	aryl
Boc	*t*-butoxycarbonyl
Bu	butyl
˚C	degrees centigrade
cat.	catalyst
Cet	cetyl (hexadecyl)
conc.	concentration
D	distribution ratio
d	doublet (NMR)
δ	chemical shift
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
E	percent extraction
eq	equivalent, equilibrium
Et	ethyl
g	gram(s)
GC	gas chromatography
h	hour(s)
Hex	hexyl
HLW	high-level radioactive wastes
HPLC	high-performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
ICP-AES	inductively coupled plasma atomic emission spectrometry
IR	infrared
J	coupling constant (NMR)
L	litter(s)
Ln	lanthanide
M	molar concentration, metal
m	milli, multiplet (NMR)
μ	micro

MA	minor actinide
Me	methyl
min	minute(s)
mol	mole(s)
mp	melting point
NBS	*N*-bromosuccinimide
NIPA	*N*-isopropylacrylamide
NMR	nuclear magnetic resonance
Ph	phenyl
ppm	parts per million
Pr	propyl
q	quartet
R	alkyl
rt	room temperature
s	singlet (NMR)
sat.	saturated
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TPEN	*N*,*N*,*N*',*N*'-tetrakis(pyridin-2-yl- methyl)ethylenediamine
wt.	weight

Chapter I

General Introduction

I-1 Introduction

Reduction of radioactive toxicity of high level liquid waste (HLW) is very important to decrease the risk of the environmental impact of nuclear wastes that is disposed deep underground. If several long-lived radioactive nuclides containing actinides are removed from HLW before the final disposal, these nuclides can be converted to short lived ones by transformation technology using neutron by fast reactor or accelerator. The environmental load of HLW will be reduced largely by the introduction of transmutation technology. However, lanthanides, whose total amount corresponding to up to 30 times that of actinides in HLW, adversely affect the efficiency of the actinide transmutation, because the transmutation target must be minimized for economic reasons and lanthanides absorb a large proportion of neutron owing to the large adsorption cross section. Therefore, the separation of actinides from lanthanides is one of the essential subjects to improve the transmutation However, it is well known that separating trivalent actinides (An^{3+}) from lanthanides (Ln^{3+}) is one of the most challenging issues, because of their similarity in chemical properties. To develop the valuable extractants is an important task for the application of

the innovative chemical separation techniques to the reprocessing of the spent nuclear fuel and the partitioning of the HLW. In the field of the nuclear chemical engineering, of great importance is in the selective separation of An^{3+}, which enables long-lived An^{3+} to reduce its toxicity by transmutation with neutron. This thesis focuses on development efficient extractant for americium(III) with organic solvent.

The Author would like to contribute to solving of the problem of the nuclear waste management by developing useful chelating agent which be able to separate of actinides and lanthanides.

In this chapter, the Author briefly reviews the several research for the synthesis of new chelating agent.

I-2 Liquid-Liquid extraction for separation of metal ion

Solvent extraction is a highly versatile method, applicable in procedures ranging from laboratory scale separations to large scale operation. Therefore, this technique belongs to the most important process for the separation and purification of various metal ions. The extractant plays a key role in the extraction efficiency and the separation operation. The

selection of an appropriate extractant often determines the success of an extraction process.

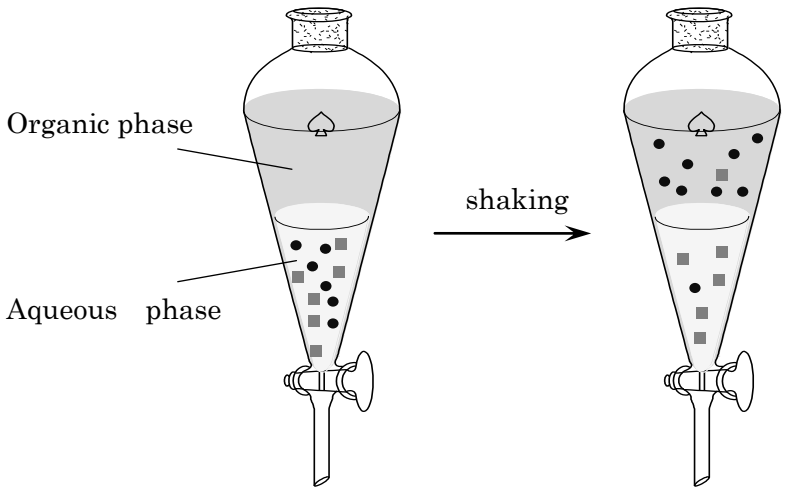
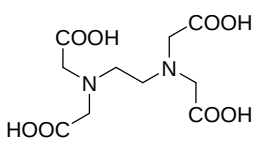
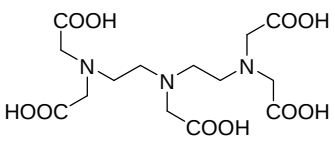


Fig. 1 Concept of solvent extraction

EDTA(**1**), which is ethylenediamine tetracarboxylic acid and efficiently binds to metal with *N* and *O* donors, is a well known chelating agent for a variety of metal ions. Approximately 50,000 tons of aminopolycarboxylates such as EDTA and the related DTPA(**2**) are used annually; mainly in the textile, detergent and pulp and paper industries.



EDTA (**1**)
Ethylenediaminetetraacetic Acid



DTPA (**2**)
Diethylene Triamine Pentaacetic Acid

Chart 1

Solvent extraction technique also plays a important role in hydrometallurgy, where nuclear technology represents the crucial field. One of the topics attracting attention in recent decades is removal of long-lived, highly toxic isotopes of minor actinides (mainly americium and curium) from HLW as a nitric acid solution.

I-3 Separation of Americium(III) from Lanthanid(III)

Currently, about 15% of the world's electricity is generated by over 400 nuclear power plants. Number of the Nuclear power plant is likely to increase in order to meet future energy needs. As a consequence, the large quantities of nuclear waste depositories will continue to expand. In recent decades a great deal of research has been devoted to the subject of the practical nuclear waste management in order to reduce its burden on the environment. Nevertheless, there is no satisfactory solution to this problem and the need for reducing current and future waste disposal remains to be unsolved. Nuclear waste management processes that are presently in operation start with the PUREX process,[1] in which almost all uranium and plutonium are separated from the depleted fuel. The residual waste stream

HLW contains the remaining fission products along with minor actinides Np, Am, and Cm. The long lasting radioactivity ($T_{1/2}$ = 10^3 -10^4 years) of these elements makes storage of HLW a serious environmental problem such as risk of leaking therefore, this problem economically unfavorable. The radiotoxicity of HLW can be reduced by transmutation of the minor actinides into short-lived ($T_{1/2}$ = 10^1 years) nuclides or stable nuclides. However, the lanthanides (especially Sm, Gd, and Eu) which also exist in HLW have high neutron capture cross sections and preferably absorb the neutrons compared to the actinides. For a satisfactory transmutation process it becomes imperative to separate the actinides from the chemically similar but relatively harmless lanthanides.

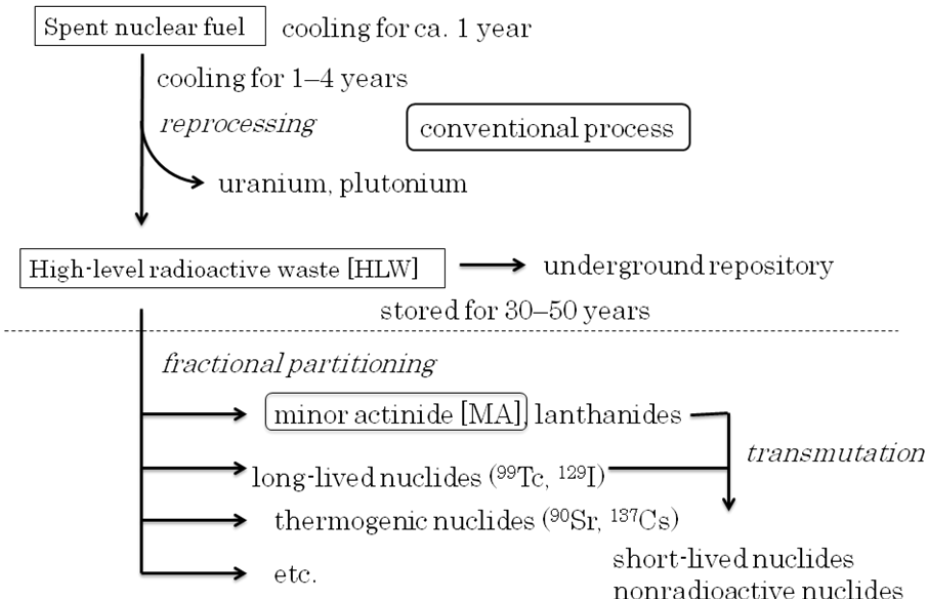


Figure 1 Partitioning and Transmutation of high-level radioactive waste.

This separation is one of the most challenging issues, owing to the very similar physicochemical properties of An^{3+} and Ln^{3+}. Indeed, lanthanides and transplutonium actinides both exist predominantly in their trivalent oxidation states in solution. They are hard acids in Pearson classification[2] (HSAB for Hard and Soft Acids and Bases) with close ionic radii. There interaction with inorganic and organic ligands are therefore predominantly determined by electrostatic and steric factors.

Even if both An^{3+} and Ln^{3+} are considered to be hard acids in HSAB theory, the higher spatial expansion of 5f actinide orbitals with respect to the 4f lanthanide orbitals opens possibility to discriminate them through their relative hardness. Therefore, it was pointed out by Musikas in the 1980s that extractant molecules containing nitrogen or sulfur functionalities which are softer than oxygen donors offered great potential to achieve the wanted discrimination.[3] Interestingly, sulfur-based soft donor extractants like bisalkyldithiophosphinic acids have been developed by Zhu and have given excellent separation factors.[4]

Therefore, considerable effort have been devoted to the development of new soft donor extractant for separating An^{3+} from Ln^{3+}.[5]

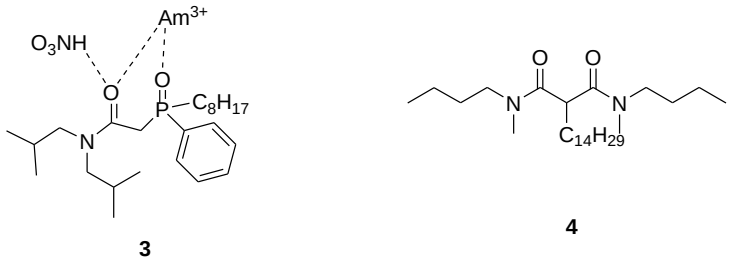
I-3-2 An^{3+} ligands

The extensive research into proper nuclear waste management of the past decades has led to development of a large number of An^{3+} ligands. The extraction ability and stability of the complexes formed with these ligands are characterized by their distribution ratio (*D*), defined as the ratio between the metal concentration in the organic and in the aqueous phase at their equilibrium. The separation factor, defined as the quotient of the distribution ratios, indicates the complex extractability and stability with respect to the second metal. In the following sections ligands that are mostly encountered or that have a noteworthy complexation behavior will be highlighted.

I-3-3 *O*-donating ligands

This group of ligands covers a broad range of *O*-bearing functionalities (viz. phosphonates, phosphinates, phosphine oxides, amides, carbonic acids, ketones, pyridine *N*-oxides, and phenols). Carbamoylmethylphosphonates and the carbamoylmethylphosphine oxides derivatives of the latter (**3**, Chart 2) are well known presently used for chelating agent in the TRUEX (transuranium extraction) process.[6] Upon

complexation with the metal cation this ligand forms a six-membered chelate with, in general, a ligand to metal stoichiometry of 1 : 3.7. It is believed that this ligand predominantly coordinates with its phosphoric oxygen and the carbonyl oxygen only weakly coordinates to the metal cation, but functions as an internal buffer and coordinates with a proton. The strength of the formed complexes for these types of *O*-donors are generally phosphine oxide > phosphate > phosphonate.



3 **4**

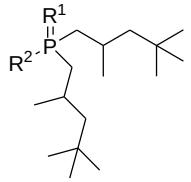
Chart 2

N,N'-Dimethyl-*N,N'*-dibutyl-tetradecylmalonamide **4** is currently used in the DIAMEX process[7] for the sequestering of actinides and lanthanides. The malonamide ligands have the advantage of being completely incinerable and thus fulfill the CHON-principle (ligands that consist only of carbon, hydrogen , oxygen, and nitrogen atoms are preferred, since they produce less harmful waste after incineration) leading to diminished secondary wastes. The malonamides coordinate in a bidentate

fashion with their carbonyl oxygens. Their extraction efficiency is generally increased upon increasing the nitric acid concentration resulting in a maximum D_{Am} at around 8 M HNO_3. The *O*-donor ligands are generally strong extractants owing to the hard nature of the oxygen atom. Although, *O*-donor ligands usually lack discrimination between Am^{3+} and Eu^{3+}, resulting in relatively low $SF_{Am/Eu}$ values.

I-3-4 *S*-donating ligands

Cyanex 301 (**5**, Chart 3) is a good example of an Am^{3+} chelator having a very high $SF_{Am/Eu}$ due to the strong–covalent binding of Am^{3+} to the relatively softer sulfur donor atom.



R^1 = S, R^2 = SH (Cyanex 301) (**5**)
R^1 = S, R^2 = OH (Cyanex 302) (**6**)
R^1 = O, R^2 = OH (Cyanex 272) (**7**)

Chart 3

A difference of -25.6 kJ mol^{-1} was observed between the enthalpies of Am^{3+} and Eu^{3+} extraction by **5** into kerosene.[8] **5** shows $SF_{Am/Eu}$ values over one thousand are found, however, the selectivity is considerably lowered of Cyanex 302 (**6**) and Cyanex 272 (**7**) which permit an examination of changes

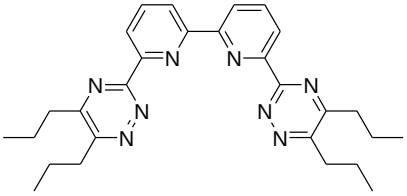
in the solution stoichiometries of Ln^{3+} and An^{3+} complexes as the ligand donor arrays change from O donor to soft S donor sets.

As a result, the applicability of the compound of this type for use in the industrial process decreases. No shortening in the Am–S bonds was found compared to the Ln–S bonds in extracted complexes. Whether the differences in structure and stoichiometries of the extracted An and Ln complexes contribute to the high selectivity of **5** is not yet fully understood. The use of synergistic mixtures with *O*- or *N*-donating ligands, the D_{Am} is greatly improved. With 2,2'-bipyridyl or 1,10-phenanthroline auxiliary ligands $SF_{Am/Eu}$ values of over 40000 are obtained resulting from the combination of two softer Lewis bases. The synergistic mixtures also suffer from oxidation and protonation at lower pH, resulting in strong decreases of D_{Am}.

I-3-5 *N*-donating ligands

With regard to extraction efficiency and Am^{3+} selectivity the *N*-donor ligands are placed more or less in between the *O*- and *S*-donor ligands. In most *N*-donor ligands, the nitrogen atom is incorporated into an aromatic ring. Ligands based on pyridine, pyrimidine, pyrazine,

1,2,4-triazine, 1,3,5-triazine, 1,2,4-triazole, benzimidazole, benzothiazole, and benzoxazole ring systems in various combinations have been studied for Am^{3+} extraction and also have been studied for complex properties. The 1,2,4-triazine-pyridine ligands **8** and **9** (Chart 4) possess the highest D_{Am} (>100) and $SF_{Am/Eu}$ (>100) values in the nitrogen donor ligands up to now.[9] These values are obtained at a nitric acid concentration of 1 M, which is relatively high for *N*-donor type of ligands which are rather easily protonated. The high preference of **8** and **9** for Am^{3+} complexation is believed to originate from the two adjacent nitrogen atoms in the 1,2,4-triazine rings. These two nitrogens possess a partial charge that is considerably lower than that of the nitrogens in a 1,3,5-triazine ring (0.312 *e* versus 0.559 *e*) which essentially means a softer characteristics for the two adjacent nitrogens and thus a more covalent Am^{3+} binding. Besides the electronic nature of the coordinating atoms, there is also an important role have the ligand structure and complexation geometry.



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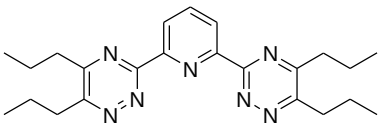
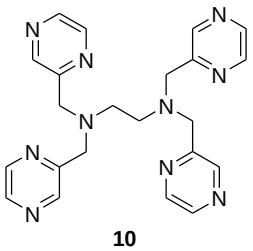


BTB (**9**)

Chart 4

10 and **11** (Chart 5) was demonstrated by the large difference in the $SF_{Am/Eu}$ values of ligands which have different spatial orientations of their coordinating groups.[10] Stronger *N*–metal bonds are formed in **10** owing to the ability of the ligand which possess nitrogen atoms in the pyrazine ring are the preferred complexation geometry more closely resulting in an approximately 30 times higher $SF_{Am/Eu}$.

Furthermore, due to the chelate effect, extraction efficiencies are also generally better for ligands having a higher multivalency as shown in ligand TPEN (*N,N,N',N'*-tetrakis(2-pyridylmethyl)ethylenediamine) ($SF_{Am/Eu}$ >100).[11] Such ligands are also able to replace all coordinated water molecules and to encapsulate the ligand creating a lipophilic exterior which facilitates phase transfer. This is one of the most predominant reasons for the high extraction efficiency of ligands **8** and **9** which coordinate in a 2 : 1 and 3 : 1 ligand to metal stoichiometry, respectively.[12]



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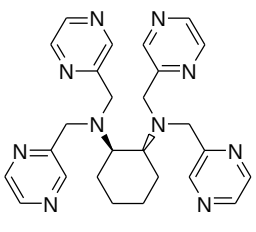

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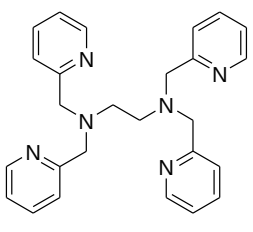


TPEN (**12**)

Chart 5

I-4 TPEN *N,N,N',N'*-tetrakis(2-pyridylmethyl)ethylenediamine

Encapsulating metal ions with a podand-type ligand is an attractive field in supramolecular chemistry and has a high-potentiality for the metal separation. In particular, a podand type ligand is useful for formation of stable complex of f-block metal ion with high coordination number, because water molecules coordinating strongly around the metal ion are removed by the encapsulation of the metal with a podand-type ligand and the encapsulated metal ion is shielded from the attack of water molecules. One strategy being pursued to apply the podand-type ligand to the separation of trivalent actinide (An) from lanthanide (Ln).

Nitrogen-containing heterocyclic based multidentate ligands have been more presently attracted by their combustibility.[13] As a consequence of this criteria, considerable efforts have been devoted to the development of new ligands for separating Am^{3+} from Ln^{3+}.[14] The first successful nitrogen based soft donor ligand is 5-methyl-2-(2-pyridyl)benzimidazole (MPIM) (**13**). However, this ligand requires thiocyanate ion as a co-ligand to achieve good selectivity of Am^{3+} over Ln^{3+}. The only type of the ligand that shows good selectivity between Am^{3+} and Ln^{3+} without any co-ligand is

2,6-di(5,6-dipropyl-1,2,4-triazin-3-yl)pyridine (BTP) (**9**) and its analogues. A problem of this ligand is its chemical stability under its extraction conditions.

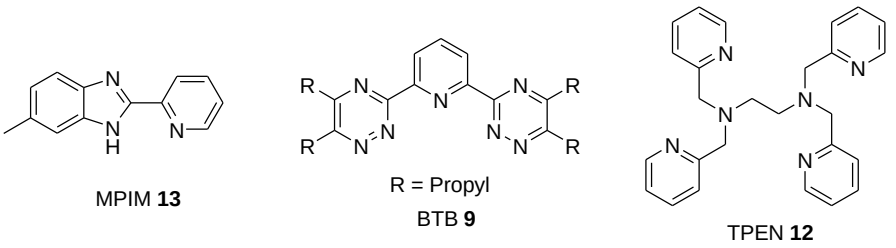


Chart 6

TPEN(**12**) is a hexadentate ligand with six nitrogen donors, as shown in Chart 6. It is well known that soft metals such as Hg, Cd, Au and Pd, which are classified by Pearson's HSAB principle[2] are complexed selectively with a soft-donor ligand containing nitrogen or sulfur, Jensen et al. studied the complex formation of Am^{3+} and Eu^{3+} with TPEN in an aqueous solution and determined the stability constants to be about 100. TPEN recognized the slight difference in the softness between Am^{3+} and Eu^{3+}. Takeshita et al. proposed and tested the synergistic extraction process of soft metals with TPEN, in which an organophosphoric acid or a carboxylic acid is used as a coextractant.[15]

These studies demonstrated that TPEN, analog with its masking

properties, is an excellent extractant for soft metals. However, due to the enhanced solubility of the protonated TPEN in the acidic aqueous phase pH<4, the extraction performance of TPEN suffers in this region. The application of TPEN to practical process is restricted, because of the high solubility of protonated TPEN to the acidic aqueous phase.

Cordier et al. reported that the hydrophobicity of a nitrogen-donor extractant was improved by introducing hydrophobic groups to the compound and that the extraction separation of Am^{3+} and Eu^{3+} was attained successfully in highly acidic solutions.[14] Takeshita et al. suggested that the extraction performance of TPEN is reduced remarkably by the introduction of alkyl groups into the molecular framework (N-C-C-N structure). The positioning of alkyl functional groups is very important to preserve TPEN's extraction performance and its selectivity for soft metals.[16]

Our resent work suggested that introduction of hydrophobic substituents onto the pyridine rings of TPEN would be a solution of such problems concerning the extraction of metal ions and found that TPEN derivatives bearing alkoxy groups somewhat improved the extraction performance of Cd^{2+} ion from acidic aqueous solution.[17] However, the acidic

tolerance of hydrophobic TPEN was found to be far from satisfactory and we recognized that further improvement of hydrophobic characteristics of TPEN derivatives with molecular design based on organic synthesis is desirable.

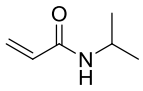
I-5 Thermal –Swing extraction using thermal sensitive polymer gel.

Solvent extraction technique is applicable to the treatment process of nuclear waste, However, since large amount of chemicals are supplied to these solvent extraction processes. To use of solvent extraction technique have to be managed safely as the secondary radioactive wastes. The consumption of chemicals should be suppressed from the viewpoint of the decrease of economical protection.

Recently, a thermal swing extraction system using thermosensitive polymer gel was proposed. A thermosensitive polymer gel is shrunken at higher than LCST (lower critical solution temperature) and swollen at less than LCST. Metal ion are captured on functional ligands copolymerized in the gel at the shrinking state and are released by the deformation of the configurational change of functional ligands by the volume phase transition of gel from the shrinking state to the swelling one. The complex formation

between metal ions and the formational ligands may be affected strongly by the volume phase transition of thermosensitive gel is applied to the elution process of metal ions, If the thermal-swing operation using thermosensitive gel is applied to the elution process of metal ions, a quantity of eluent for the recovery of metal ions may be reduced considerably.

Poly(*N*-isopropylacrylamide) is a representative of thermosensitive polymers and has a LCST in the vicinity of 33 ºC in water,[18] it exhibits hydrophilicity and hydrophobicity in water at temperatures lower and higher than the LCST, respectively.



NIPA
N-isopropylacrylamide (**14**)

The NIPA hydrogel swells below the LCST, and it shrinks and its copolymer have attracted a great deal of attention for their potential applications in drug delivery systems,[19] biosensors,[20] microfluidic actuators,[21] etc. Takeshita et al. proposed a new extraction technique called thermal-swing extraction, in which a thermosensitive gel copolymerized with functional ligands is prepared and the extraction and elution of object material are controlled by the conformational change of these functional

ligands with the volume phase transition of thermosensitive gel. Therefore, the object material can be recovered without adding new chemicals. The consumption of chemicals can be reduced substantially by introducing the thermal-swing extraction technique. For example, the concept of thermal-swing extraction can be realized by a *N*-isopropylacrylamide(NIPA) gel copolymerized with a functional ligand monomer. Previously, some NIPA gels copolymerized with a phosphoric acid ester and a BTP[2,6-di(3-vinylbenzyl-1,2,4-triazol-5-yl)pyridine] were synthesized and the thermal-swing extraction of heavy metals such as lanthanide, actinide, and transient elements was tested.[22] The recent extracdtion tests of Cd^{2+} using the NIPA-BTP gel indicated that the thermal-swing extraction was attained successfully and the extractability of BTP was controlled in principle by the temperature response Cd^{2+} between the swelling state (5°C) and the shrinking one (40°C) was only 4 times. In this performance, it is difficult to establish a practical thermal-swing extraction process. For the increase in the difference of extrability between high and low temperatures, the conformation of functional ligands introduced in the gel should be changed substantially with temperature. The use of TPEN as a functional

ligand instead of BTP was considered to get the clear conformational change with temperature. Four pyridyl groups in TPEN are flexible and the steric conformation of 6 nitrogen donors may be changed easily by the volume phase transition of thermosensitive gel. Figure2 shows the concept of thermal-swing extraction process using thermosensitive gel with an encapsulating ligand such as TPEN.

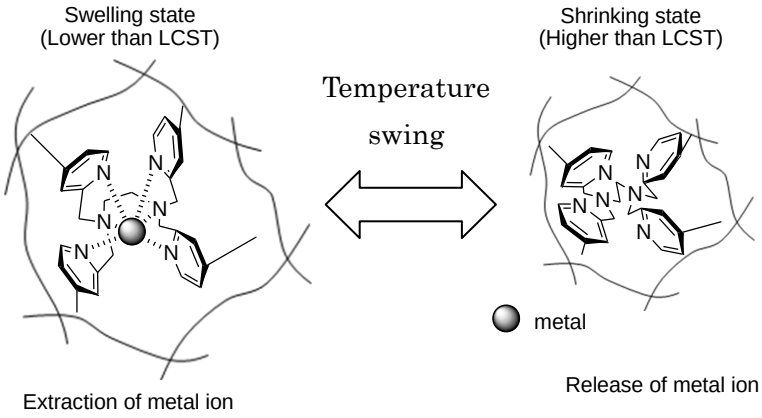


Figure 2 Concept of thermal-swing extraction.

Takeshita et al. synthesized a TPEN derivative combining propenyloxy group to four pyridyl groups, TPPEN [*N,N,N',N'*-tetrakis(4-propenyloxy-2-pyridylmethyl)ethylenediamine] was synthesized to introduce TPEN in thermoseisitive gel. Thermal-swing extraction of Cd^{2+} with a thermosensitive gel, poly (*N*-isopropylacrylamide) (NIPA) crosslinked with an encapsulating ligand, TPPEN, was examined. Cd^{2+} was extracted in the gel swollen at 5 ºC and released from the gel

shrunken at 40 ºC. The difference in the distribution ratio of Cd^{2+} between these temperatures was more than 30 times.[23]

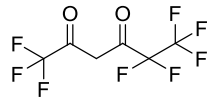
Our further concern is the relationship of the formation of polymer gel with the number of the terminal polymerizable double bond and the effect of the chain length of the spacer between double bond and pyridine ring and the effect of the structure of 1,2-ethylendiamin moiety.. It is intriguing to study the relation between the structure and the function.

I-6 Metal extraction from water into fluorous solvent

Fluorocarbons attract much interest in a wide range of fields in organic chemistry, biochemistry, and material science due to its unique properties.[24] The solubility of fluorous solvents in water is extremely low and similar to but generally lower than conventional organic solvents, fluorous solvents are likely tobe potential candidates for novel separation media in metal extraction. Nevertheless, only a few papers have reported use of fluorous solvents as separation media for metal ions.

Maruyama et al. reported a liquid-liquid extraction system based on perfluorocarbon(fluorous-solvent extraction) that allows selective extraction

of metal ions from aqueous and organic phases to perfluorocarbon phase (FC-72) with perfluorinated β-diketone(**15**).[25]



β-diketone**15**

Chart 7

A metal extraction system using fluorous solvent is intriguing, in particular, extraction of minor actinides with a fluorous solvent can be a new class of solvent extraction system.

I-7 Purpose of this thesis

Solvent extraction, which is an important unit operation in the industry field, has been applied widely to the separation on notable metals, biochemical , materials and environmental pollution. This thesis studied for design and synthesis of novel chelating agent to separate trivalent actinides from trivalent lanthanides. This is a key step in partitioning and transmutation strategy of nuclear waste, which is one of the important matter that should be considered for the future management of nuclear waste. one of the scenarios being a seriously considered for the future management of nuclear waste.

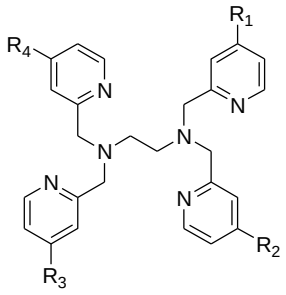
TPEN derivatives bearing polymerizable functional group are synthesized, and copolymerization of NIPA with TPEN as a crosslinker is carried out. The relationship of gels to the cross-linker structure and extraction behavior of Cd^{2+} are investigated.

The Author also attempts to synthesize the TPEN derivatives bearing fluoroalkyl subustituent and extraction ability of Cd^{2+} with the TPEN derivatives are studied.

I-7-1 Chapter II

This chapter describes that syntheses of TPEN derivatives bearing the different number of the terminal double bond, formation of polymer gels, and extraction studies of a Cd^{2+} with the synthesized polymer TPEN gel.

TPEN derivatives with the different number of terminal double bond were synthesized and subjected to copolymerization with NIPA. The polymer gels composed of **1**, **2**, and **4** were found to be obtained and showed thermo responsive swelling and shrinking behaviors.

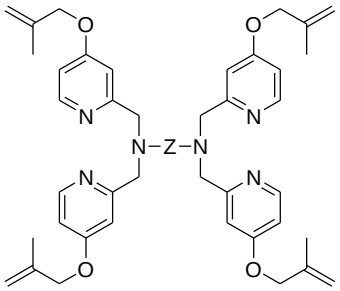


	R_1	R_2	R_3	R_4
TPEN	H	H	H	H
1	allyl-O-	allyl-O-	allyl-O-	allyl-O-
2	allyl-O-	allyl-O-	allyl-O-	H
3	allyl-O-	allyl-O-	H	H
4	allyl-O-	H	allyl-O-	H
5	allyl-O-	H	H	H

Figure 3 The structures of TPEN and TPEN derivatives bearing polymerizable functional group.

I-7-2 Chapter III

This chapter describes the study on the effect of the structure of 1,2-ethylenediamine moiety of TPEN. We report synthesis of several TPEN derivatives with different diamine structure, radical copolymerization of thus prepared TPEN derivatives and NIPA, and studies on the temperature-dependent extraction of Cd^{2+} ion with thus obtained TPEN-NIPA gel derivatives.



	Z
1	$(CH_2)_2$
2	$(CH_2)_3$
3	$(CH_2)_2O(CH_2)_2$

Figure 4 Structure of TPEN derivatives 1-3

I-7-3 Chapter IV

This Chapter describes synthesis of several TPEN derivatives bearing polymerizable functional group at the 4-position of the pyridine ring, and copolymerization of NIPA with TPEN as a crosslinker. The relationship of gels to the cross-linker structure and extraction behavior of Cd^{2+} are investigated.

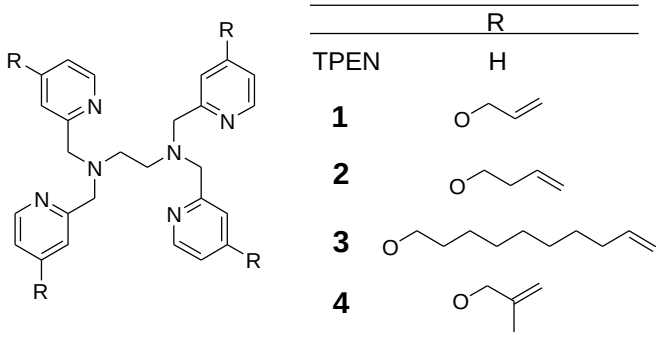
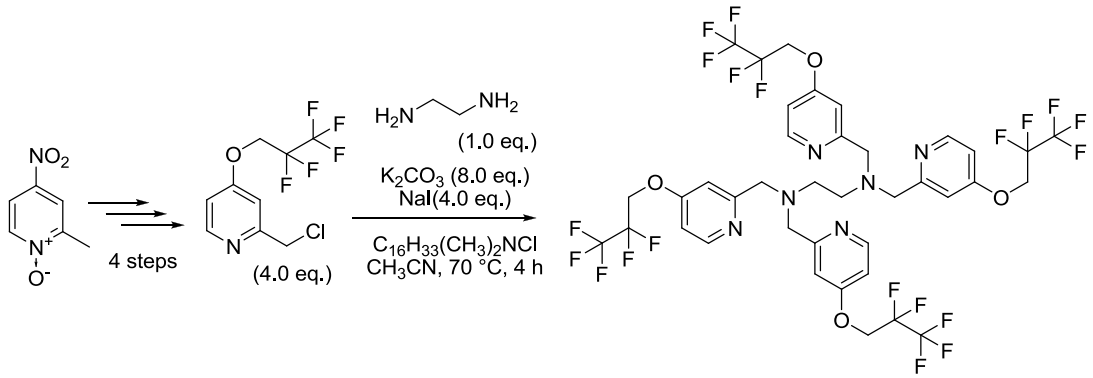


Figure 5 The structures of TPEN derivatives bearing polymerizable functional group.

I-7-4 Chapter V

This Chapter describes that synthesis of TPEN derivatives bearing fluoroalkyl substituent and its extraction behavior of metal ion. Novel TPEN derivatives bearing fluoroalkyl substituents at the 4-position of the pyridine ring are synthesized and extraction ability of Cd^{2+} with the TPEN derivatives are studied. The fluorinated TPEN derivative exhibited excellent extraction performance particularly from highly acidic aqueous solution. Extraction of Am^{3+} was also conducted.



Scheme 1. Synthesis of the fluorinated TPEN derivative.

Extraction behavior of Cd^{2+}at pH 1.0

	E%
TPEN	5
New chelating agent	84

Water phase : $[Cd]_{init}$: 1 mM, pH controlled : HNO_3.
Organic phase : [TPEN derivative] : 1 mM, solv. : $CHCl_3$.

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Chapter II

Thermo-responsive extraction of Cd^{2+} with TPEN-NIPA gel. Effect of the Number of Polymerizable Double Bond Towards Gel Formation and the Extracting Behavior

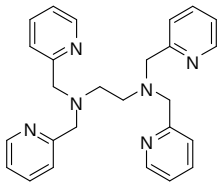
Abstract: *N,N,N',N'*-(Tetrakis-2-pyridylmethyl)ethylenediamine (TPEN) derivatives bearing the different number (1–4) of a double bond moiety on the pyridine ring are synthesized and subjected to copolymerization with *N*-isopropylacrylamide in the presence of AIBN. The obtained poly(TPEN-NIPA) gels show thermoresponsive swelling/shrinking behaviors and are employed for the extraction of cadmium(II) ion from the aqueous solution to examine the relationship of the gel characteristics and the extraction performance. The polymer gels composed of the TPEN derivative bearing three or four double bonds exhibit temperature dependent change of swelling and shrinking inwater. These gels extract Cd^{2+} ion efficiently from the aqueous solution in the swelling state at 5 °C, while little extraction was observed at 45 °C with shrinking.

II-1 Introduction

Solvent extraction technique has been of considerable interest and extensively applied for separation of metal ions with a chelating agent. Organic molecules composed of multiple nitrogen atoms are particularly important for the extraction of soft metals,[1] such as Hg, Cd, Au and Pd, and development of separation for d- or f-block metals has been an attractive issue. A wide range of chelating agent has been developed so far for the purpose of separation of, for example, minor actinides (MA) from high level radioactive wastes (HLW).[2] TPEN, which is *N,N,N',N'*-(tetrakis-2-pyridylmethyl) ethylenediamine **1** suggested to be a hexadentate ligand with six nitrogen atoms to chelate a metal ion,[3] is a potential candidate for the practical and selective extracting agent for MAs from HLW.[4] Much effort has been paid to the use of TPEN for the extraction, however, difficulties on the practical use of TPEN is its highly water soluble and ease of protonation characteristics under acidic conditions. Accordingly, incorporation of the TPEN structure into a side chain of polymers is a method to avoid leaching into water phases during extraction.

On the other hand, the polymer of *N*-isopropylacrylamide (NIPA) has

attracted interesting characteristics, that is, water soluble at low temperature and becomes hydrophobic by raising the temperature to higher than ca. 35 °C.[5] Thereby, the corresponding poly- NIPA gels show thermo-responsive swelling/shrinking behaviors on that temperature and have applied for metal extraction using temperature-dependent change of chelation ability.[6] Accordingly, change of extraction characteristics of TPEN derivatives induced by the thermo-responsive behaviors of such gel is intriguing if poly- NIPA gel is prepared with a cross-linker, in which TPEN moiety is incorporated.



TPEN (**1**)

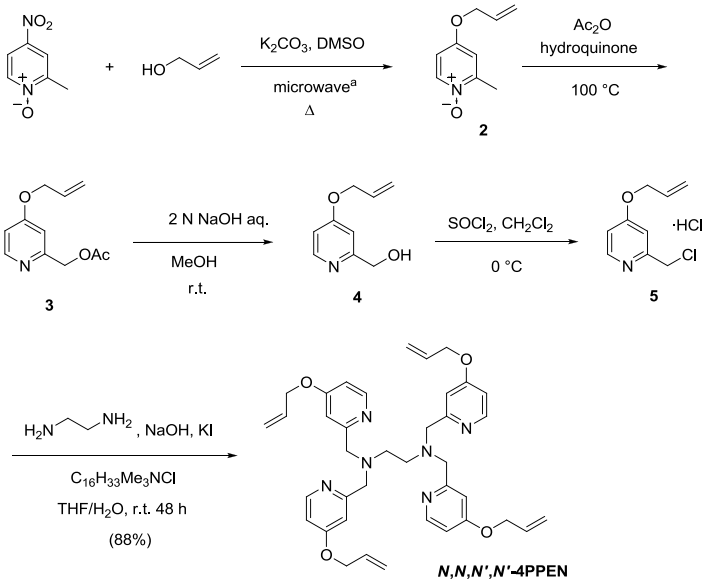
In our previous works, we have shown that a TPEN-NIPA gel was synthesized by radical polymerization of NIPA in the presence of a TPEN derivative bearing four polymerizable double bonds on the pyridine ring and showed temperature-dependent change of extraction behavior of Am^{3+} and Cd^{2+}, which was recognized as a model metallic species of MAs.[7] The TPEN-NIPA gel effectively extracted Cd^{2+} ion at swelling state (5 °C), while little extraction of Cd^{2+} ion was confirmed at the elevated temperature (45

°C) where shrinking of the gelwas observed.[7] Our further concern has focused on the relationship of the formation of polymer gel with the number of the terminal polymerizable double bond, which would be highly important toward improved molecular design of the polymer gel. We herein report syntheses of TPEN derivatives bearing the different number of the terminal double bond, formation of polymer gels with such TPENs, and studies on temperaturedependen extraction behaviors of a Cd^{2+} ion[8] with the obtained TPEN-NIPA gel.

II-2 Result and discussion

Synthesis of TPEN derivatives bearing the different number of the polymerizable functional group was carried out as outlined in Schemes 1 and 2. The synthetic strategywas based on the controlled introduction of functionalized and unsubstituted chloromethylpyridine derivatives into ethylenediamine. Chloromethylpyridine bearing an allyloxy group at the 4-position of the pyridine ring 5 was prepared in a manner as described previously with a slight modification from commercially available 2-methyl-4-nitro-pyridine 1-oxide and allyl alcohol and used as hydrochloride,

which was isolated directly from the mixture of the reaction of hydroxymethylpyridine **4** with thionyl chloride (Scheme 1)

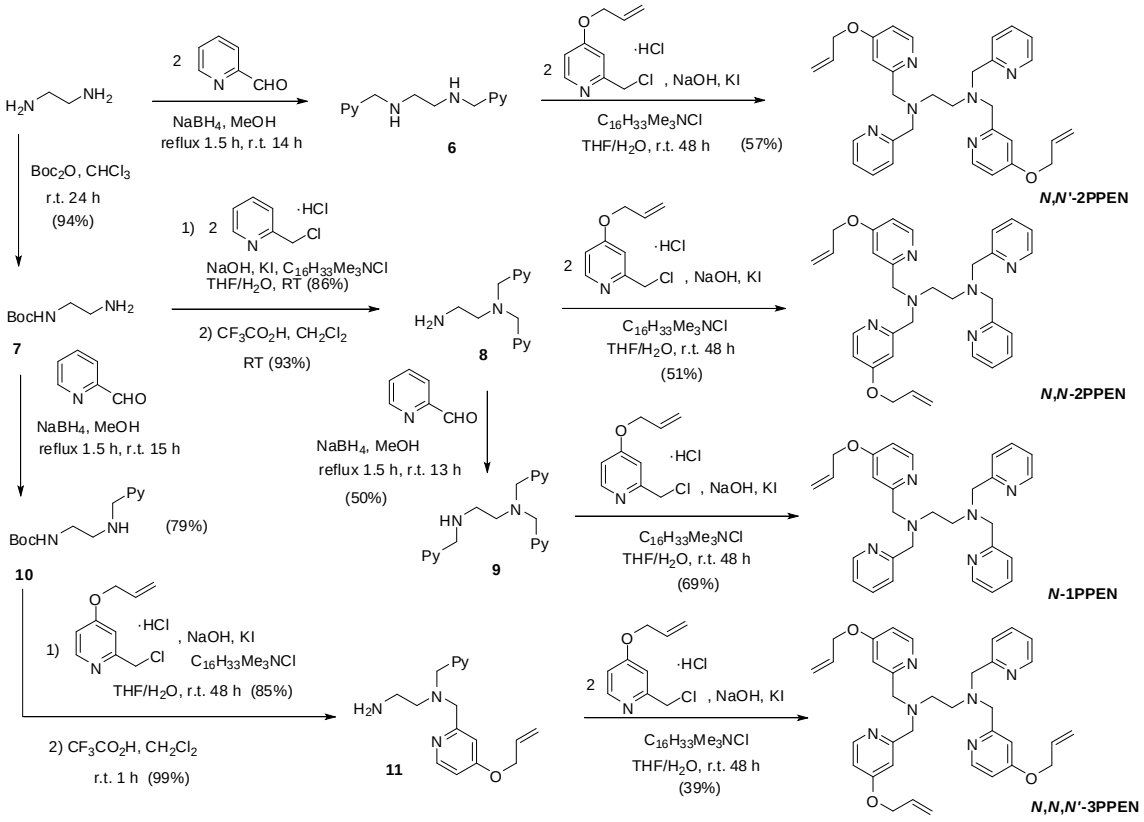


Scheme 1.

Reductive amination of 2-pyridinecarbaldehyde with ethylenediamine lead to (*N,N'*-pyridylmethyl)ethylenediamine **6**, which was employed for the following reaction without further purification. The following reaction of **5** and **6** in a biphasic THF/water system in the presence of NaOH, KI, and a catalytic amount of $C_{16}H_{33}Me_3NCl$ (2 mol %) at room temperature afforded symmetric *N,N'*-bifunctionalized TPEN derivative *N,N'*-2PPEN in 57% overall yield. Other TPEN derivatives were synthesized with *N*-Boc-ethylenediamine **7**, which was prepared by the reaction of ethylenediamine with $(Boc)_2O$.[10] The reaction of **7** with chloromethylpyridine

hydrochloride in the manner for the reaction of **6** and **5** and following removal of the Boc group afforded *N,N*-difunctionalized compound **8** in an excellent yield. On the other hand, reductive amination of 2-pyridinecarbaldehyde with **8** lead to **9**, which was further treated with 5 in a similar manner to the reaction of **5** and **6** afforded mono-functionalized derivative *N*-1PPEN in 69% yield. Reductive amination of 2-pyridinecarbaldehyde with **7** afforded **10**. The reaction of **10** with **5** and following removal of Boc furnished **11**. Treatment of the obtained **11** with **5** afforded the TPEN derivative bearing three double bonds *N,N,N'*-3PPEN. All of the TPEN derivatives bearing the different number of the double bond were synthesized in reasonable yields. Worthy of note is the modified protocol of the reaction of chloromethylpyridine with an amino group. Conventional synthesis of TPEN has been performed by the reaction of chloromethylpyridine **5** with ethylenediamine in aqueous NaOH to result in giving considerably poor yield (<30%). Although the method was effective for the unsubstituted chloromethylpyridine, the use of the allyloxy derivative induced a variety of side reactions leading to the formation of inseparable byproducts. Employment of biphasic reaction in the presence of a phase

transfer catalyst and addition of potassium iodide, which would cause in situ transformation of chloride on the pyridine ring into iodide was found to cause drastic improvement of the yield of TPEN derivatives.[13] Subsequently, the improved synthetic method resulted to give well-defined TPEN derivatives with the different number of allyloxy group in a reasonable yields. (Scheme 2).



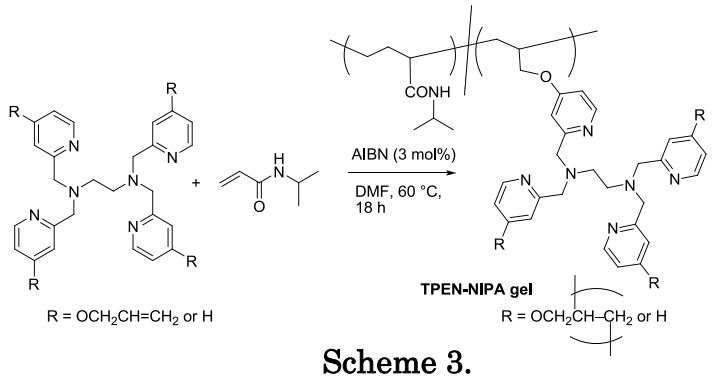
Scheme 2.

We then carried out formation of TPEN-NIPA gel with the obtained derivatives. The polymerization was performed by radical polymerization with AIBN as an initiator in DMF in the presence of 1.25 mol % of TPEN

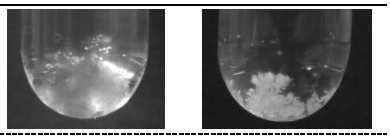
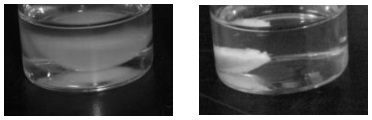
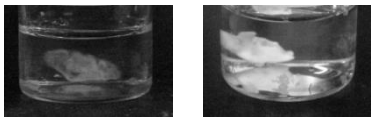
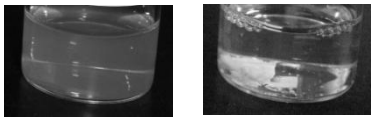
derivatives ***N,N'*-2PPEN**, ***N,N'*-2PPEN**, ***N,N,N'*-3PPEN**, and ***N,N,N',N'*-4PPEN**[7] (Scheme 3). All of the polymerization proceeded within 18 h at 60 °C. Insoluble polymer gels were obtained by the reaction of TPEN derivatives bearing three or four polymerizable double bonds. As shown in Table 1, the obtained polymer gel derived from ***N,N,N'*-3PPEN** showed swelling in water at room temperature and heating the gel in water at 45 °C resulted to exhibit shrinking. These behavior was similar to the case of ***N,N,N',N'*-4PPEN**.[7] On the other hand, the polymer synthesized with ***N,N'*-2PPEN** bearing symmetric two terminal double bonds was found to give partially water-soluble gel. Although increasing the amount of TPEN to 2.5 mol % resulted to afford the gel of better quality, slow leaching was observed by standing the polymer gel in water at room temperature. By contrast, gellation with ***N,N'*-2PPEN** under similar conditions was found to be unsuccessful to observe dissolving in water within a few days. These results suggest that employment of the TPEN derivative bearing more than three allyloxy group is necessary to obtain the polymer gel and the *N,N'*-difunctionalized derivative is preferable for gellation compared to the *N,N*-difunctional one. Although the gellation might be possible when two

polymerizable functional group exists, more than two double bonds in the TPEN derivative is preferable to form stable polymer gel. The findings would be due to the inferior reactivity in the radical polymerization of unfunctionalized C–C double bond to acrylamide. With the polymer gel bearing the TPEN moiety in hand, extraction studies were performed using a cadmium(II) ion employing the dried TPEN gel by the removal of water under reduced pressure. We first examined the temperature-dependent extraction performance of TPEN-NIPA gels in the swelling state (5 ºC) and the shrinking state (45 ºC) at the pH value of 2.1 and 5.3, respectively. As summarized in Figure 1, the percent extraction value (%*E*) of CdII ion at each temperature and pH with TPEN-NIPA gels, in which 1.25 mol % of the corresponding TPEN derivative is incorporated, was estimated by ICP-AES analysis. The calculation of %*E* was based on the assumption that all of the TPEN derivative was incorporated into the polymer gel in the copolymerization. Both ***N,N,N'*-3PPEN** and ***N,N,N',N'*-4PPEN** extracted the cadmium(II) ion at 5 ºC highly efficiently, while the extraction performance at 45 ºC was much inferior to those at 5 ºC. The results suggest that excellent extraction of cadmium(II) ion is observed in the swelling state, while the gel

hardly extracted Cd^{2+} in the shrinking state at 45 ºC. A slightly higher extraction at 45 ºC was observed with ***N,N,N'*-3PPEN** bearing three double bonds than with ***N,N,N',N'*-4PPEN** suggesting that TPEN bearing the less number of the double bond still involved freedom to chelate the metal ion even in the shrinked state to cause inferior temperature-dependent difference of extraction. Such an extraction behavior was also observed at pH 2.1 although the percent extraction value was found to be lower. TPEN-NIPA gel ***N,N,N',N'*-4PPEN** extracted ca. 23.2% of Cd^{2+}at 5 ºC, while no extraction was observed at the shrinking state (45 ºC). On the other hand, ***N,N,N'*-3PPEN** composed of the three polymerized moiety exhibited inferior thermo-responsive behavior. Since actual separation of minor actinides is performed in an acidic aqueous solution, the thermo-responsive extraction behavior at the pH value of 2.1 is particularly noteworthy.



Scheme 3.

TPEN derivative	(mol%)	polymer	thermo-responsive change[c]
***N,N,N',N'*-4PPEN**	(1.25)[b]	gel (completely insoluble in water)	
***N,N,N'*-3PPEN**	(1.25)	gel (completely insoluble in water)	
***N,N'*-2PPEN**	(1.25)	partially water soluble	
	(2.50)	gel (slow leaching)	
***N,N*-2PPEN**	(2.5)	water soluble	

[a] Polymerization was carried out with NIPA (1.5 mmol), AIBN (3 mol%), and TPEN in 0.13 mL of DMF at 60 ºC for 18 h. [b] Prepared in a manner shown in ref 6. [c] Swelled (left); shrinked (right).

Table 1. Radical polymerization of NIPA with TPEN derivatives with the different number of polymerizable double bond and thermo-responsive behaviors of the obtained TPEN-NIPA gel.

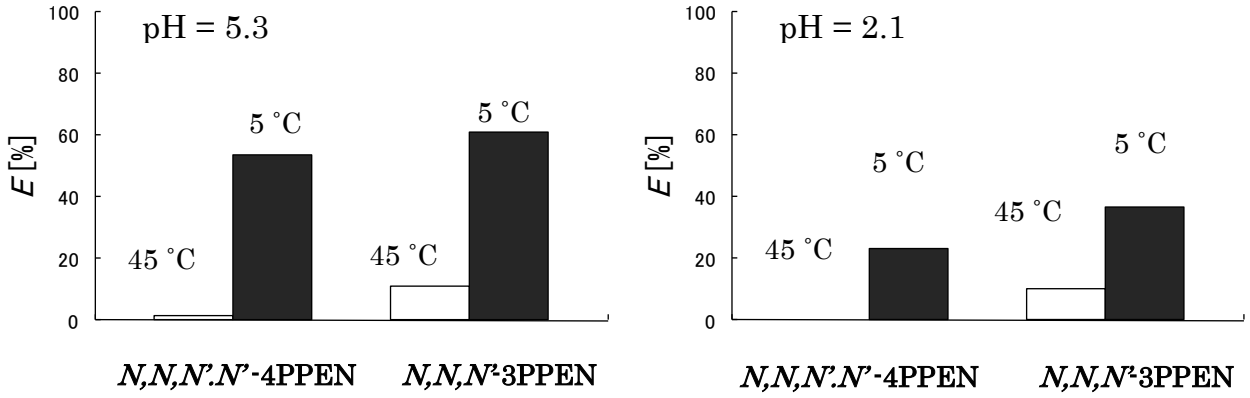


Figure 1. Temperature-dependent extraction of Cd^{2+} ion with *N,N,N',N'*-4PPEN-NIPA gel and *N,N,N'*-3PPEN-NIPA gel at pH 5.3 (left) and pH 2.1 (right).

II-3 Conclusion

In summary, we have synthesized TPEN derivatives bearing the different number of polymerizable allyloxy group and the prepared derivative was subjected to the formation of TPEN gel. When the derivative bearing three and *N,N'*-difunctionalized two allyloxy group was found to form the polymer gel in addition to the case of tetrakis-functionalized TPEN. Among these, polymer gels composed of three or four polymerizable double bond on TPEN showed temperature-dependent extraction behaviors. The TPEN-NIPA gel composed of ***N,N,N'*-3PPEN** exhibited superior extraction performance at low temperature although the thremo-responsive change of extraction was inferior to ***N,N,N',N'*-4PPEN**, while ***N,N,N',N'*-4PPEN-NIPA** gel showed the excellent temperature-dependent change with slightly lower extraction.

II-4 Experimental

General

NMR (500 MHz for ^{1}H, 125 MHz for ^{13}C) spectra were recorded on a Bruker Avance 500 spectrometer at the Center for Supports to Research and Education Activities, Kobe University. Chemical shifts are expressed in ppm using tetramethylsilane as an internal standard (0 ppm). Coupling constants (*J*) were shown in Hertz (Hz). IR (ATR) spectra were measured with Brucker Optics Alpha with Ge. TLC analyses were performed on analytical TLC plates coated with 60 F_{254} (E. Merck) silica gel or alumina on aluminum foil. Column chromatography was performed using silica gel Wakogel C200 (Wako Chemicals Co. Ltd.) or basic alumina (Wako Chemicals Co. Ltd or Merck). High-resolution mass spectra were measured at Nara Institute of Science and Technology with JEOL JMS-700. ICP-AES analysis was carried out with SII SPS3100 at the Center for Supports to Research and Education Acitivities of Kobe University.

Tetrahydrofuran (anhydrous grade) was purchased from Wako Chemicals Co. Ltd. and stored in a Schlenk tube under a nitrogen

atmosphere. Other chemicals were purchased and used without further purification.

Materials

DMSO was purchased from Wako Pure Chemical Industries, Co. Ltd. as an anhydrous grade and stored in a Schlenk tube under nitrogen atmosphere. Other chemicals were purchased and used as such. Preparation of palladium complex **2a-c**, **3a** and **4a** and platinum complexes **6d-e** and $[PtX_2(bpy)]$ (X = Cl, I) were performed by methods shown in the literature.[8, 10, 11, 12]

4-(Prop-2-en-1-yloxy)-2-picoline 1-oxide (2)

To a 20 mL of round-bottle flask was added 4-nitro-2-picoline 1-oxide (494.3 mg, 3.2 mmol) in allyl alcohol (5 mL). The mixture was heated until to homogeneous was dissolved in allyl alcohol, and then potassium carbonate (493.2 mg, 3.6 mmol) was added. The reaction mixture was stirred at 100 ˚C for 7 h. Allyl alcohol was removed under the reduced pressure, then the residue was poured into water and extracted with $CHCl_3$. The extract was washed with water, dried over anhydrous Na_2SO_4 and concentrated in vacuo

to afford **2** (584.2 mg) (>99%). The product was used in the next step without further purification.

2-Chloromethyl-4-(prop-2-en-1-yloxy)pyridine hydrochloride (5)

To a 300 mL of round-bottom flask was added compound **2** (5.8 g, 35 mmol) in acetic anhydride (60 mL) and the mixture wad stirred at 100 ˚C for 3 h. Acetic anhydride was evaporated under the reduced pressure, then the residue was basified with sat. Na_2CO_3 aq. and extracted with $CHCl_3$. The extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel (30:1–20:1 *n*-hexane:EtOAc) to afford 4-(prop-2-en-1-yloxy)pyridin-2-ylmethyl acetate (**3**, 5.6 g, 27 mmol) in 77% yield. To a 200 mL of round-bottom flask was added compound **3** (5.6 g, 27 mmol) in methanol (42 mL) and 1 M NaOH aq. (28 mL, 28 mmol) at room temperature. The reaction mixture was stirred at the same temperature for 1.5 h. The solvent was evaporated and the residue was extracted with $CHCl_3$. The extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo to yield [4-(prop-2-en-1-yloxy)pyridin-2-yl]methanol (**4**, 3.5 g, 21 mmol) (78%). To a solution of compound **4** in CH_2Cl_2 was added thionyl chloride in CH_2Cl_2 dropwise at 0 °C, After stirring for 2 h at 0 ºC,

large amount of diethyl ether was added and the solvent was evaporated to afford hydrochloride salt. ^{1}H NMR (methanol-d_4) δ 4.93 (s, 2H), 4.96 (td, J = 1.4, 5.4 Hz, 2H), 5.43 (dd, J = 1.3, 10.7 Hz), 5.53 (dd, J = 1.3, 17..4 Hz), (6.08–6.15 (m, 1H), 7.51 (dd, J = 2.6, 6.9 Hz, 1H), 7.67 (d, J = 2.6 Hz, 1H), 8.65 (d, J = 6.9 Hz, 1H). HRMS (EI+) found: m/z 183.0452. Calcd for 183.0451 (as dehydrochlorinated product:$C_9H_{10}ClNO$).

N,N,N',N'-Tetrakis[4-(prop-2-en-1-yloxy)pyridin-2-ylmethyl]ethylenediamine (N,N,N',N'-4PPEN): General procedure for alkylation of ethylenediamine with 2-(chloromethyl)pyridines hydrochloride in THF/H_2O

To a test tube equipped with a magnetic stirring bar were added ethylenediamine (20.1 μL, 0.3 mmol), 2-(chloromethyl)pyridine hydrochloride **5** (264.1 mg, 1.2 mmol), hexadecyltrimethylammonium chloride (1.9 mg, 0.006 mmol), NaOH (96.0 mg, 2.4 mmol), THF (0.6 mL) and H_2O (0.6 mL). KI (199.2 mg, 1.2 mmol) was then added, and the resulting mixture was stirred vigorously at room temperature for 48 h. The reaction mixture was extracted with CH_2Cl_2 and the extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on alumina using 30:1 $CHCl_3$-MeOH as an eluent to

afford 0.17 g of ***N,N,N',N'*-4PPEN** as a pale yellow oil (88% yield). ^{1}H NMR ($CDCl_3$) δ 2.86 (s, 4H), 3.80 (s, 8H), 4.50 (d, J = 5.4 Hz, 8H), 5.29 (dd, J = 1.2, 10.4 Hz, 4H), 5.37 (dd, J = 1.2, 17.4 Hz, 4H), 5.94–6.02 (m, 4H), 6.66 (dd, J = 2.2, 5.7 Hz, 4H), 7.05 (d, J = 2.2 Hz, 4H), 8.27 (d, J = 5.7 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 52.3, 60.5, 68.4, 108.9, 109.2, 118.4, 132.1, 150.0, 161.2, 165.3. HRMS (EI+) found: m/z 648.3428. Calcd for 648.3424.

N,N'-Bis[4-(prop-2-en-1-yloxy)pyridin-2-ylmethyl]-N,N'-bis(pyridin-2-ylmethyl)ethylenediamine (*N,N'*-2PPEN)

To a 50 mL of two-neck flask were added compound ethylenediamine (0.34 mL, 5 mmol), molecular sieves 3A (0.50 g) in MeOH (10 mL) under a nitrogen atmosphere. A solution of pyridine-2-carboxyaldehyde (0.95 mL, 10 mmol) in MeOH (10 mL) was added slowly, and the mixture was refluxed for 1.5 h. After cooling to room temperature, $NaBH_4$ (567.5 mg, 15 mmol) was added to the mixture, which was stirred overnight at room temperature. After removal of molecular sieves, the solvent was evaporated. The residue was dissolved in sat. Na_2CO_3 aq. and extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford

crude *N*,*N*'-bis(pyridin-2-ylmethyl)ethylenediamine (**6**)[9] (1.23 g). The product was used in the next step without further purification.

To a test tube were added compound **6** (72.7 mg, 0.3 mmol), **5** (132.1 mg, 0.6 mmol), hexadecyltrimethylammonium chloride (1.9 mg, 0.0006 mmol) and NaOH (48.0 mg, 1.2 mmol) in THF (0.6 mL) and H_2O (0.6 mL). KI (99.6 mg, 0.6 mmol) was then added, and the resulting mixture was stirred vigorously at room temperature for 48 h. The reaction mixture was extracted with CH_2Cl_2 and the extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on alumina ($CHCl_3$:MeOH = 30:1) to afford ***N*,*N*'-2PPEN** (92.4 mg, 0.17 mmol) in 57% yield. ^{1}H NMR ($CDCl_3$) δ 2.96 (s, 4H), 3.91 (s, 8H), 4.53 (d, J = 5.2 Hz, 4H), 5.31 (dd, J = 1.3, 10.4 Hz, 2H), 5.39 (dd, J = 1.3, 17.2 Hz, 2H), 5.96–6.03 (m, 2H), 6.69 (dd, J = 2.2, 5.8 Hz, 2H), 7.11–7.13 (m, 4H), 7.44 (d, J = 7.7 Hz, 2H), 7.57 (td, J = 1.7, 7.7 Hz, 2H), 8.28 (d, J = 5.8 Hz, 2H), 8.46 (d, J = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 52.2, 60.5, 60.6, 68.3, 108.6, 109.0, 118.2, 121.8, 122.6, 132.0, 136.2, 148.8, 149.9, 159.4, 161.4, 165.1. HRMS (EI+) found: m/z 536.2900. Calcd for 536.2903.

(2-Aminoethyl)carbamic acid *tert*-butyl ester (7)[10]

To a 300 mL of round-bottom flask was added ethylenediamine (13.4 mL, 200 mmol) in $CHCl_3$ (100 mL). A solution of di-*tert*-butyl dicarbonate (4.4 g, 20 mmol) in $CHCl_3$ (50 mL) was added dropwise over a period of 2 h at 0 °C. After stirring at room temperature for 24 h, the mixture was washed with brine. The organic layer was washed with water, dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford compound **7** (3.0 g, 18.8 mmol) as a colorless oil in 94% yield. ^{1}H NMR ($CDCl_3$): 1.36 (s, 9H), 1.80 (s, 2H), 2.74 (t, J = 5.8 Hz, 2H), 3.11 (q, J = 5.4 Hz, 2H), 4.89 (br s, 1H).

_N,N_-Bis(pyridin-2-ylmethyl)ethylenediamine (8)[11]

To a test tube equipped with a magnetic stirring bar were added **7** (320.4 mg, 2 mmol), 2-chloromethylpyridine hydrochloride (656.1 mg, 4 mmol), hexadecyltrimethylammonium chloride (12.8 mg, 0.04 mmol), NaOH (320 mg, 8 mmol), THF (4 mL), and H_2O (4 mL). KI (664.0 mg, 4 mmol) was then added, and the resulting mixture was stirred vigorously at room temperature for 48 h. The reaction mixture was extracted with CH_2Cl_2 and the extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on alumina (hexane:EtOAc = 1:1) to afford

{2-[bis(pyridin-2-ylmethyl)amino]ethyl}carbamic acid *tert*-butyl ester (586.2 mg, 1.7 mmol) in 86% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.43 (s, 9H), 2.77 (br s, 2H), 3.23 (br s, 2H), 3.93 (s, 4H), 5.86 (br s, 1H), 7.17 (dd, J = 5.0, 6.5 Hz, 2H), 7.45 (d, J = 7.5 Hz, 2H), 7.65 (t, J = 7.5, Hz, 2H), 8.55 (d, J = 5.0 Hz, 2H).

To a 100 mL of round-bottom flask was added {2-[bis(pyridin-2-ylmethyl)amino]-ethyl}carbamic acid *tert*-butyl ester (1.2 g, 3.4 mmol) in CH_2Cl_2 (10.3 mL). Trifluoroacetic acid (17.2 mL) was added dropwise over a period of 30 min at 0 °C. After stirring at room temperature for 1 h, solvent was evaporated, then the residue was dissolved in aq. NaOH and extracted with CH_2Cl_2. Organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford compound **8** (0.77 g, 3.2 mmol) (93%). ^{1}H NMR ($CDCl_3$): 2.41 (br s, 2H), 2.60 (t, J = 6.0 Hz, 2H), 2.73 (t, J = 6.0, Hz, 2H), 3.75 (s, 4H), 7.03 (ddd, J = 1.0, 4.8, 7.6 Hz, 2H), 7.36 (d, J = 7.6 Hz, 2H), 7.53 (td, J = 1.9, 7.6 Hz, 2H), 8.42 (ddd, J = 1.0, 1.9, 4.8 Hz, 2H).

_N,N_-Bis[4-(prop-2-en-1-yloxy)pyridin-2-ylmethyl]-_N',N'_-bis(pyridin-2-ylmethyl)ethylenediamine (_N,N_-2PPEN)

To a test tube equipped with a magnetic stirring bar were added compound **8** (72.7 mg, 0.3 mmol), **5** (132.1 mg, 0.6 mmol),

hexadecyltrimethylammonium chloride (1.9 mg, 0.0006 mmol) and NaOH (48.0 mg, 1.2 mmol), THF (0.6 mL), and H_2O (0.6 mL). KI (99.6 mg, 0.6 mmol) was then added, and the resulting mixture was stirred vigorously at room temperature for 48 h. The reaction mixture was extracted with CH_2Cl_2 and the extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on alumina (EtOAc:MeOH = 20:1) to afford ***N,N*-2PPEN** (82.8 mg, 0.15 mmol) in 51% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.75–2.77 (m, 4H), 3.72 (s, 4H), 3.77 (s, 4H), 4.49 (td, *J* = 1.4, 5.3 Hz, 4H), 5.28 (dd, *J* = 1.3, 10.6 Hz, 2H), 5.37 (dd, *J* = 1.3, 17.3 Hz, 2H), 5.94–6.02 (m, 2H), 6.65 (dd, *J* = 2.5, 5.7 Hz, 2H), 7.04 (d, *J* = 2.5 Hz, 2H), 7.08 (ddd, *J* = 1.0, 4.9, 7.5 Hz, 2H), 7.43 (d, *J* = 7.5 Hz, 2H), 7.55 (td, *J* = 1.7, 7.5, 2H), 8.28 (d, *J* = 5.7 Hz, 2H), 8.46 (d, *J* = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 52.2, 52.3, 60.55, 60.62, 68.3, 108.6, 108.9, 118.2, 121.7, 122.6, 132.0, 136.2, 148.8, 149.9, 159.5, 161.5, 165.1. HRMS (EI+) found: m/z 536.2900. Calcd for 536.2901.

N,N,N'-Tris(pyridin-2-ylmethyl)ethylenediamine (9)[11]

To a 25 mL of round-bottom flask were added compound **8** (242.3 mg, 1 mmol), pyridine-2-carboxyaldehyde (94.8 μL, 1 mmol) and 3 Å molecular

sieves in MeOH (4 mL). The reaction mixture was refluxed for 1.5 h, and cooled to room temperature. $NaBH_4$ (113.5 mg, 3 mmol) was added to the mixture, which was stirred overnight at room temperature. After removal of molecular sieves, solvent was evaporated to leave a crude oil, which was purified by column chromatography on alumina using MeOH as an eluent to afford **9** (165.2 mg, 0.50 mmol) in 50% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.87 (s, 4H), 3.84 (s, 4H), 3.94 (s, 2H), 7.12 (ddd, *J* = 1.1, 4.9, 7.5 Hz, 2H), 7.16 (ddd, *J* = 1.1, 4.9, 7.5 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 2H), 7.60 (td, *J* = 1.7, 7.6 Hz, 2H), 7.64 (td, *J* = 1.7, 7.6 Hz, 1H), 8.48 (d, *J* = 4.9 Hz, 2H), 8.50 (d, *J* = 4.9 Hz, 1H).

_N_-[4-(Prop-2-en-1-yloxy)pyridin-2-ylmethyl]-_N,N',N'_-tris(pyridin-2-ylmethyl) ethylenediamine (N-1PPEN)

To a test tube equipped with a magnetic stirring bar were added compound 9 (100.0 mg, 0.3 mmol), 5 (66.0 mg, 0.3 mmol), hexadecyltrimethylammonium chloride (1.9 mg, 0.0006 mmol), NaOH (24.0 mg, 0.6 mmol), THF (0.6 mL), and H2O (0.6 mL). KI (49.8 mg, 0.3 mmol) was then added, and the resulting mixture was stirred vigorously at room temperature for 48 h. The reaction mixture was extracted with CH2Cl2 and

the extract was dried over anhydrous Na2SO4 and concentrated in vacuo. The residue was purified by column chromatography on alumina (EtOAc:MeOH = 20:1) to afford N-1PPEN (99.8 mg, 0.21 mmol) in 69% yield. 1H NMR (CDCl3, 500 MHz): δ 2.76 (s, 4H), 3.73 (s, 2H), 3.76 (s, 2H), 3.77 (s, 4H), 4.50 (td, J = 1.5, 5.4 Hz, 2H), 5.30 (dd, J = 1.3, 10.6 Hz, 1H), 5.39 (dd, J = 1.3, 17.2 Hz, 1H), 5.96–6.03 (m, 1H), 6.66 (dd, J = 2.4, 5.8 Hz, 1H), 7.06 (d, J = 2.4 Hz, 1H), 7.09–7.12 (m, 3H), 7.43 (d, J = 7.6 Hz, 1H), 7.44 (d, J = 7.6 Hz, 2H), 7.56 (td, J = 1.7, 7.6 Hz, 3H), 8.29 (d, J = 5.8 Hz, 1H), 8.47–8.48 (m, 3H); 13C NMR (CDCl3, 125 MHz): δ 52.1, 52.2, 60.4, 60.6, 68.2, 108.6, 108.9, 118.2, 121.7, 122.58, 122.61, 132.0, 136.15, 136.19, 148.70, 148.75, 149.8, 159.41, 159.42, 161.4, 165.1.HRMS found: m/z 480.2638. Calcd for 480.2635.

{2-[(Pyridin-2-ylmethyl)amino]ethyl}carbamic acid *tert*-butyl ester (10)[12]

To a 50 mL of two-neck flask were added compound **7** (801.1 mg, 5 mmol), 3 Å molecular sieves in MeOH (10 mL) under a nitrogen atmosphere. A solution of pyridine-2-carboxyaldehyde (535.6 mg, 5 mmol) in MeOH (10 mL) was added slowly, and the mixture was refluxed for 1.5 h. After cooling to room temperature, $NaBH_4$ (567.5 mg, 15 mmol) was added to the mixture, which was stirred overnight at the same temperature. After removal of

molecular sieves, the solvent was evaporated. The residue was dissolved in sat. Na_2CO_3 aq. and extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on alumina using EtOAc as an eluent to afford **10** (987.9 mg, 3.9 mmol) in 79% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.43 (s, 9H), 2.91 (t, *J* = 5.5 Hz, 2H), 3.36 (q, *J* = 5.5 Hz, 2H), 4.03 (s, 2H), 5.35 (br s, 1H), 7.21 (dd, *J* = 5.2, 7.7 Hz, 1H), 7.33 (d, 7.7 Hz, 1H), 7.67 (td, *J* = 1.7, 7.7 Hz, 1H), 8.56 (d, *J* = 5.2 Hz, 1H).

_N,N,N'_-Tris[4-(prop-2-en-1-yloxy)pyridin-2-ylmethyl]-_N'_-(pyridin-2-ylmethyl)ethylenediamine (_N,N,N'_-3PPEN)

To a test tube with ground glass were added compound **10** (251.3 mg, 1 mmol), **5** (220.1 mg, 1 mmol), hexadecyltrimethylammonium chloride (6.4 mg, 0.02 mmol) and NaOH (80.0 mg, 2 mmol) in THF (2 mL) and H_2O (2 mL). KI (166.0 mg, 1 mmol) was then added, and the resulting mixture was stirred vigorously at room temperature for 48 h. The reaction mixture was extracted with CH_2Cl_2 and the extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on aluminum oxide (Merck, 1:1 *n*-hexane:EtOAc) to afford 0.34 g of

(2-{*N*-[4-(prop-2-en-1-yloxy)pyridin-2-ylmethyl]-*N*-(pyridin-2-ylmethyl)amino }ethyl)-carbamic acid *tert*-butyl ester (85%), which was employed for the following reaction without further purification.

To a 50 mL of round-bottom flask was added (2-{*N*-[4-(prop-2-en-1-yloxy)pyridin- 2-ylmethyl]-*N*-(pyridin-2-ylmethyl) amino}ethyl)carbamic acid *tert*-butyl ester (0.34 g, 0.86 mmol) in CH_2Cl_2 (2.6 mL). Trifluoroacetic acid (4.3 mL) was added dropwise over a period of 15 min at 0 °C. After stirring at room temperature for 1 h, solvent was evaporated, then the residue was dissolved in NaOH aq. and extracted with CH_2Cl_2. Organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford compound 254 mg of *N*-[4-(Prop-2-en-1-yloxy)pyridin-2-ylmethyl]-*N*-(pyridin-2-ylmethyl)ethylene diamine (**11**, 99%).

To a test tube equipped with a magnetic stirring bar were added compound **11** (89.5 mg, 0.3 mmol), **5** (132.1 mg, 0.6 mmol), hexadecyltrimethylammonium chloride (1.9 mg, 0.0006 mmol), NaOH (48.0 mg, 1.2 mmol), THF (0.6 mL), and H_2O (0.6 mL). KI (99.6 mg, 0.6 mmol) was then added, and the resulting mixture was stirred vigorously at room

temperature for 48 h. The reaction mixture was extracted with CH_2Cl_2 and the extract was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on alumina (20:1 EtOAc:MeOH) to afford ***N,N,N'*-3PPEN** (69.9 mg, 0.12 mmol) in 39% yield. ^{1}H NMR ($CDCl_3$) δ 2.77 (s, 4H), 3.73 (s, 4H), 3.74 (s, 2H), 3.77 (s, 2H), 4.47–4.49 (m, 6H), 5.28 (td, *J* = 1.3, 10.6 Hz, 3H), 5.37 (td, *J* = 1.3, 17.3 Hz, 3H), 5.94–6.02 (m, 3H), 6.63–6.65 (m, 3H), 7.04 (d, *J* = 2.4 Hz, 3H), 7.09 (ddd, *J* = 1.2, 4.8, 7.6 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.56 (td, *J* = 1.8, 7.6 Hz, 1H), 8.26–8.28 (m, 3H), 8.47 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 52.3, 52.4, 60.60, 60.62, 60.65, 68.3, 108.5, 108.57, 108.61, 108.9, 109.0, 109.2, 118.20, 118.23, 121.8, 122.6, 131.99, 132.05, 136.2, 148.8, 149.9, 145.0, 159.5, 161.5, 165.07, 165.08. HRMS found: m/z 592.3162. Calcd for 592.3168

General Procedure for radical polymerization of NIPA with TPEN derivatives

To a 25 mL of sealed tube equipped with a magnetic stirring bar were added *N*-isopropylacrylamide (170 mg, 1.5 mmol) and TPEN derivative (0.019 mmol). The mixture was dissolved in 0.13 mL of DMF and AIBN (0.023 mol% or 0.045 mol%) was added in one portion. The resulting mixture

was heated at 60 °C for 18 h. Then, the mixture was cooled to room temperature and washed with water repeatedly. Water was removed under reduced pressure at 50 °C to leave a colorless solid. TPEN-NIPA gels obtained were found to swell at room temperature in water and shrinking was observed when the mixture was heated to 45 °C. The ratio of swelling/shrinking was 4.5-7.0 for **4PPEN**, which was estimated by the observation of the volume change of both states.

Extraction of cadmium(II) ion with TPEN-NIPA gel

A 1 mM of aqueous $Cd(NO_3)_2$ solution was prepared. The pH value of the solution was controlled to 2.1 and 5.3 by the addition of 1 M of aq. NH_4NO_3 and 1 M of HNO_3. TPEN-NIPA gel (14.5 mg; 1.25 mol% of TPEN contents), whose concentration of the TPEN moiety was controlled to be 1.5 μmol, was added to 0.75 mL of the aqueous solution. Vigorous stirring of the mixture was continued for 60 min at 0 °C or 45 °C. An aliquot of the solution (0.2 mL) was taken, passed thoruogh a membrane filter (0.2 μm), and diluted with distilled water to 4 mL, which was subjected to ICP-AES analysis. The percent extraction value was calculated as

$\%E = 100 \cdot D/(D+1)$, $\{D = ([Cd^{2+}]_{ini}-[Cd^{2+}])/[Cd^{2+}]_{ini}\}$

$[Cd^{2+}]_{ini}$: concentration of Cd^{2+} in water before extraction;

$[Cd^{2+}]$: concentration of Cd^{2+} in water after extraction.

The percent extraction values (%*E*) of ***N,N,N'*-3PPEN** were 11.1 (45 ºC) and 61.2 (5 ºC) at pH = 5.3; 10.3 (45 ºC) and 36.6 (5 ºC) at pH = 2.1, respectively, while %*E* of ***N,N,N',N'*-4PPEN**: at 1.4 (45 ºC) and 53.7 (5 ºC) at pH = 5.3; 0 (45 ºC) and 23.2 (5 ºC) at pH = 2.1

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Chapter III

Temperature-dependent change of extraction behavior of cadmium(II) ion with poly(TPEN-NIPA) gel. Effect of the chain length and branch structure of the spacer towards gel formation and the extraction

Abstract: *N*,*N*,*N*′,*N*′-(tetrakis-2-pyridylmethyl)ethylenediamine (TPEN) derivatives bearing a polymerizable double bond in the substituent structure of the pyridine ring are synthesized and subjected to copolymerization with *N*-isopropylacrylamide in the presence of AIBN. The obtained poly(TPEN-NIPA) gels show thermo-responsive swelling/shrinking behaviors and are employed for the extraction of cadmium(II) ion from the aqueous solution to examine the relationship of the gel characteristics and the extraction performance. The polymer gels composed of the TPEN derivative bearing **C3**, **C4**, **C10** and branched C3 spacer chains are synthesized and temperature-dependent extraction behavior of cadmium ion is compared. These gels extract Cd^{II} ion efficiently from the aqueous solution in the swelling state at 5 °C, while little extraction is observed at 45 °C with shrinking. It is found that poly(TPEN-NIPA) gel of branched C3 spacer (**C3b**) shows the excellent thermo-responsive extraction performance.

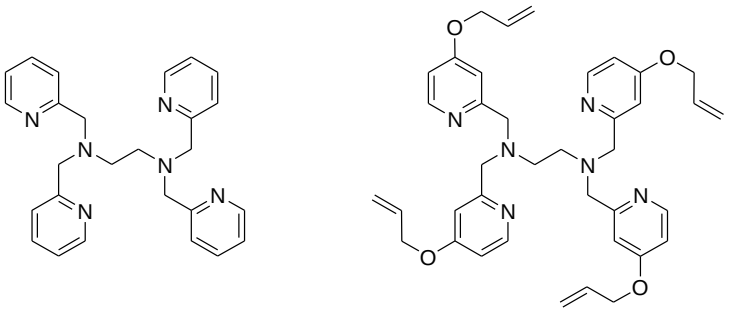
V-1 Introduction

Functionality design based on outside stimuli attracts considerable attention in a wide range of fields. A polymer gel composed of poly(*N*-isoprpyl acrylamide) (NIPA), which reversibly switch swelling and shrinking corresponding to a temperature change, is thereby intriguing as a thermo-responsive functional materials.[1] We have recently shown that poly(TPEN-NIPA) gel effectively extract soft metal ions such as Cd^{2+} and its extraction behaviors are thermally dependent in various pH regions. It was shown to extract Cd^{2+} at lower temperature, while little extraction has been observed at the elevated temperature.[2] TPEN, *N*,*N*,*N*′,*N*′(tetrakis-2-pyridylmethyl)ethylenediamine, is recognized as a hexadentate ligand with six nitrogen donors and has been shown to chelate a variety of soft metal ions such as Hg, Cd, Au, Pd, etc.[2] It was also shown to be effective for chelation of *f*block metals and separation of minor actinides from high level radioactive waste (HLW) has been an attractive issue.[3, 4] Thereby TPEN derivatives have been employed as an extracting agent for variety of metal ions in an organic solvent. On the other hand, it is possible to extract metal ions in aqueous solutions without organic solvent if the

TPEN moiety is incorporated into a polymer gel. Since poly-NIPA (*N*-isopropyl acrylamide) gel is shown to swell at low temperature in water and shrink at the elevated temperatureh higher than LCST,[1a] thermo-responsive swelling/shrinking can be applied for the corresponding conformational change of TPEN that induces temperature dependent change of extraction behaviors when the TPEN moiety such as **1a** is employed as a cross linker in the poly-NIPA gel.

In our recent report, we have studied the relationship of the number of polymerizable double bond on the pyridine ring of TPEN with the temperature-dependent extraction behavior of a cadmium(II) ion.[2c, 3] It was revealed that the poly(TPEN-NIPA) gel prepared from TPEN derivatives bearing at least three double bond moieties are necessary to form a stable polymer gel and to show temperature-dependent change of extraction behaviors. Accordingly, our concern is centered to the relationship of the chain length and branched structure of the spacer moiety between the polymer main chain and TPEN moiety. Herein, we report synthesis of several TPEN derivatives bearing four polymerizable double bond in the substituent on the pyridine ring with different methylene spacer length and

branched structure and studies on the temperature-dependent extraction behaviors of cadmium ion with poly(TPEN-NIPA) gels of the different spacer structure.[1]

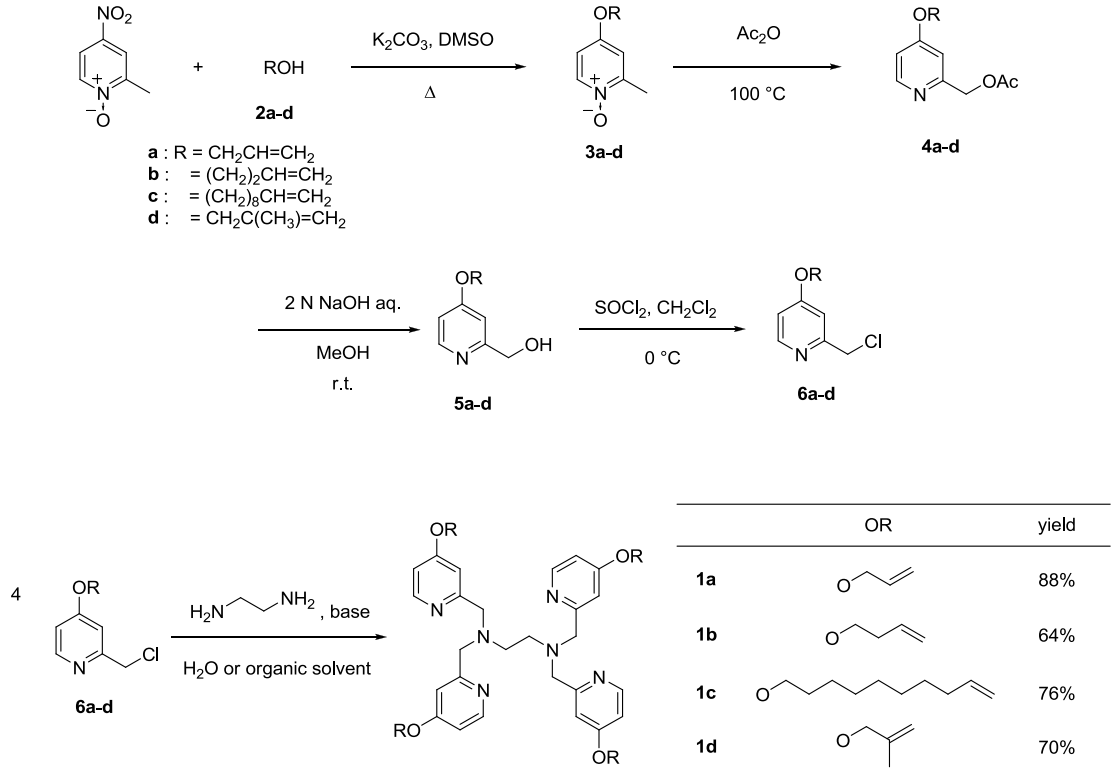


TPEN　　TPPEN (**1a**)

Results and Discussion

The synthetic pathway of TPEN derivatives with different side-chain length (**1a-c**) and branched structure (**1d**) was summarized in Scheme 1. Syntheses of pyridine derivatives bearing an allyloxy moiety **3a-6a** and the TPEN derivative **1a** were previously reported.[1] Reactions to afford **3b-d**, **4b-d**, **5b-d**, **6b-d**, were carried out in similar manners. Although the reaction of 2-methyl-4-nitropyridine-1-oxide with allylic alchohol **2a** or **2d** proceeded smoothly, harsh conditions were found to be necessary to afford **3b** and **3c**. Other reactions concerning introduction of the OAc group, hydrolysis of the acetoxy group, and chlorination proceeded similarly. The obtained chloromethyl pyridine derivatives **6** were subjected to the reaction with 1,2-ethylenediamine to afford the corresponding TPEN derivatives with

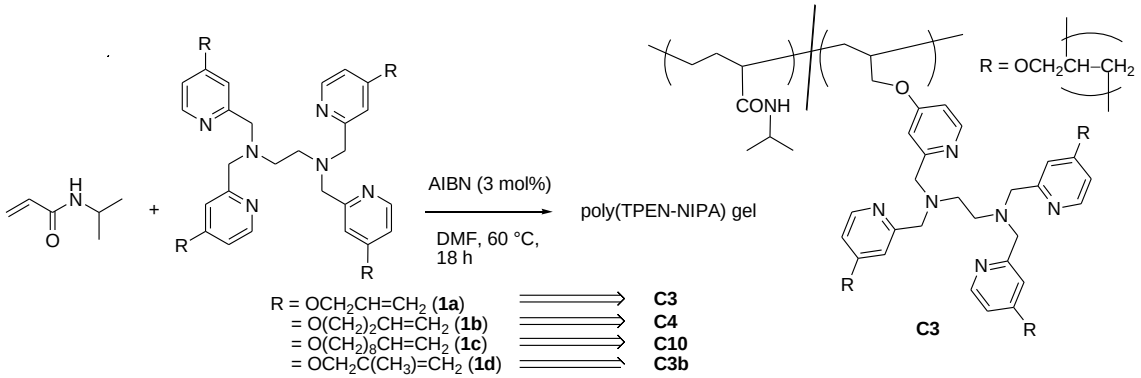
different substituents **1b-d**. The TPEN derivative **1b**, which bears 3-butenyloxy group at the 4-position of the pyridine ring, is a homologated derivative toward **1a**, while **1c** (R=9-decen-1-yl) involves longer methylene groups. On the other hand, **1d** possesses a methyl group at the C-2 carbon atom as a branched structure.



Scheme 1.

TPEN derivatives thus obtained were subjected to the radical copolymerization leading to poly(TPEN-NIPA) gel. (Scheme 2) The reaction was performed with *N*-isopropyl acrylamide (NIPA) and TPEN derivatives **1a-d** in the presence of AIBN as an radical initiator in DMF. All of the

polymerization were carried out at 60 ºC for 18 h. When 1.25 mol % of TPEN derivatives **1a, 1b** and **1d** toward NIPA were employed, the corresponding polymer gels that wereinsoluble in water were obtained.(**C3**, **C4**, **C3b**, respectively) By contrast, polymerization with **1c** resulted in insufficient gel formation and the product **C10** was mostly dissolved upon standing in water for 2 days. Improved gel formation was observed with 2.50 mol % of **1c**, however, slow leaching to water was found to be still inevitable. The obtained polymer gels were found to be insoluble to any organic solvents as well as water, thereby spectroscopic analyses of the gel to suggest the chemical structure were totally unsuccessful. Figure 1 shows poly(TPEN-NIPA) gels **C3**, **C4**, **C3b**, and **C10** in water as a swollen state.



Scheme 2.

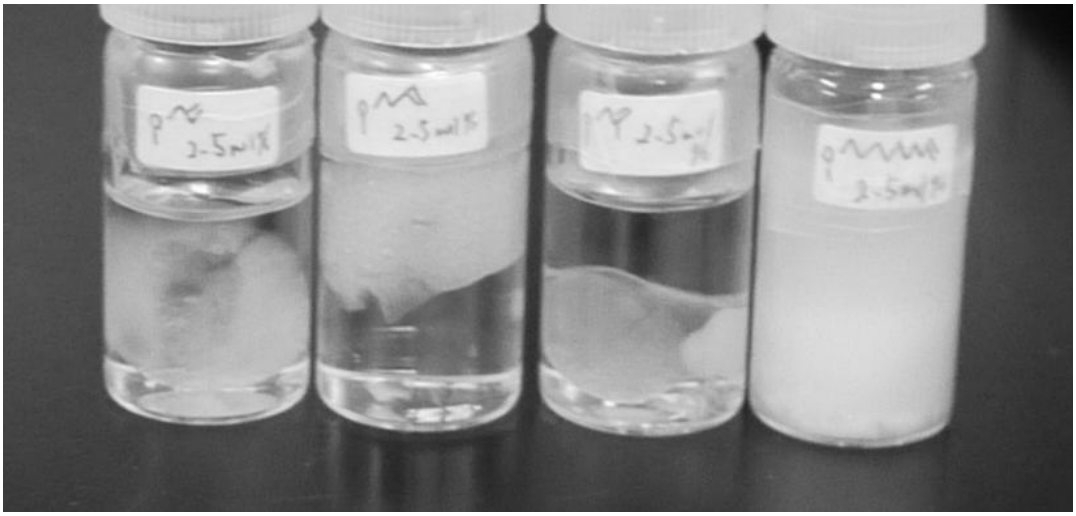


Figure 1. TPEN-NIPA gels **C3**, **C4**, **C3b**, **C10** (left to right) in water.

The obtained gels were dried with heating at 70 ºC under reduced pressure to afford colorless powders, whose aqueous solutions showed repeating swelling at room temperature and shrinking by heating. The volume change between swollen and shrinking states were found to be 25% (C3) and 18% (C10) respectively. Figure 2 shows the representative thermo-responsive change of **C4**.

Toughness of the obtained gel **C4** was mostly similar to that of **C3**. Among poly(TPEN-NIPA) gels, **C3b** was found to form the strongest gel probably due to the improved reactivity by the introduction of an electron-donating methyl substituent onto the double bond. On the other hand, the performance of poly(TPEN-NIPA) gel **C10** was inferior to other

gels to result in partially dissolving in water upon standing. This would be due to the flexible longer methylene chain that inhibited stiff cross linking.

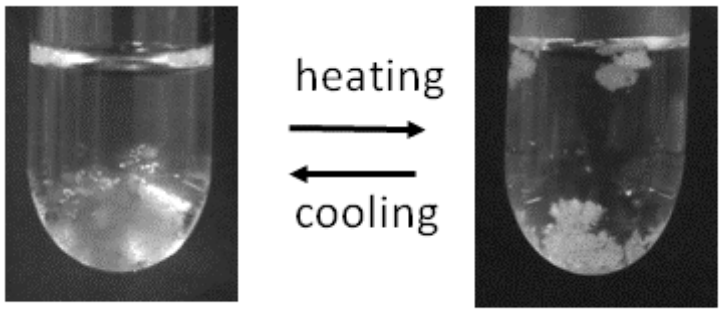


Figure 2. Thermo-responsive swelling and shrinking behaviors of **C4**.

With these poly(TPEN-NIPA) gels extraction studies were carried out using cadmium(II) ion. Temperature-dependent extraction behaviors were examined in the swollen state (5 ºC) and the shrinking state (45 ºC) at the pH values of ca. 2.0 and 6.5, respectively. A 1 mM solution of $Cd(NO_3)_2$ was prepared and the pH value was controlled to 1.9 and 5.3 (at 5 ºC), 2.0 and 5.9 (45 ºC) respectively, by the addition of NH_4NO_3. Extraction was performed by the addition of dried poly(TPEN-NIPA) gel to 0.2 mL of 1 mM solution of $Cd(NO_3)_2$. The amount of Cd^{II} ion incorporated into the gel was estimated by ICP-AES analysis of the remaining amount of cadmium ion. Figure 3 summarizes the results.

As reported previously, **C3** extracted cadmium ion efficiently at 5 °C (7.91×10^{-2} mmol-Cd/g-dry gel) when the extraction was carried out at pH = 6.5, while at 45 °C hardly extracted Cd^{2+} (0.08×10^{-2}). Such behaviors were also observed at pH = ca. 2 although the extraction performance was slightly lower (3.20×10^{-2} at 5 °C, 1.07×10^{-2} at 45 °C). **C4** was found to show slightly superior performance to **C3** in both the amount of extraction and the thermo-responsive difference (at pH = ca. 2, 4.64×10^{-2} at 5 °C, 0.48×10^{-2} at 45 °C). Such a better performance would be due to the homologation of the side chain, which improved hydrophobicity of the TPEN moiety.[5b] **C10** also showed improved performance in extraction at the pH values of both ca. 2 and 4.5 at 5 °C (5.50×10^{-2}, 9.13×10^{-2}). This would also be due to the improved hydrophobicity of long methylene chains. However, extraction in the shrinking state at 45 °C unexpectedly improved leading to the inferior thermo-responsive change at the pH of 2 and 4.5 (1.64×10^{-2}, 4.62×10^{-2}). Poly(TPEN-NIPA) gel bearing a branched structure was found to show remarkable extraction in swelling state and thermo-responsive change at pH = 6.5 to observe the highest extraction at 5 °C and little extraction at 45 °C. Worthy of note, in addition, is the remarkably high extraction at pH of 2 at 5

ºC (6.40 × 10^{-2}) and its thermo-responsive change was also excellent (6.40 × 10^{-2} to 0.26 × 10^{-2}). This would be due to the formation of stiff gel as well as the improved hydrophobicity.

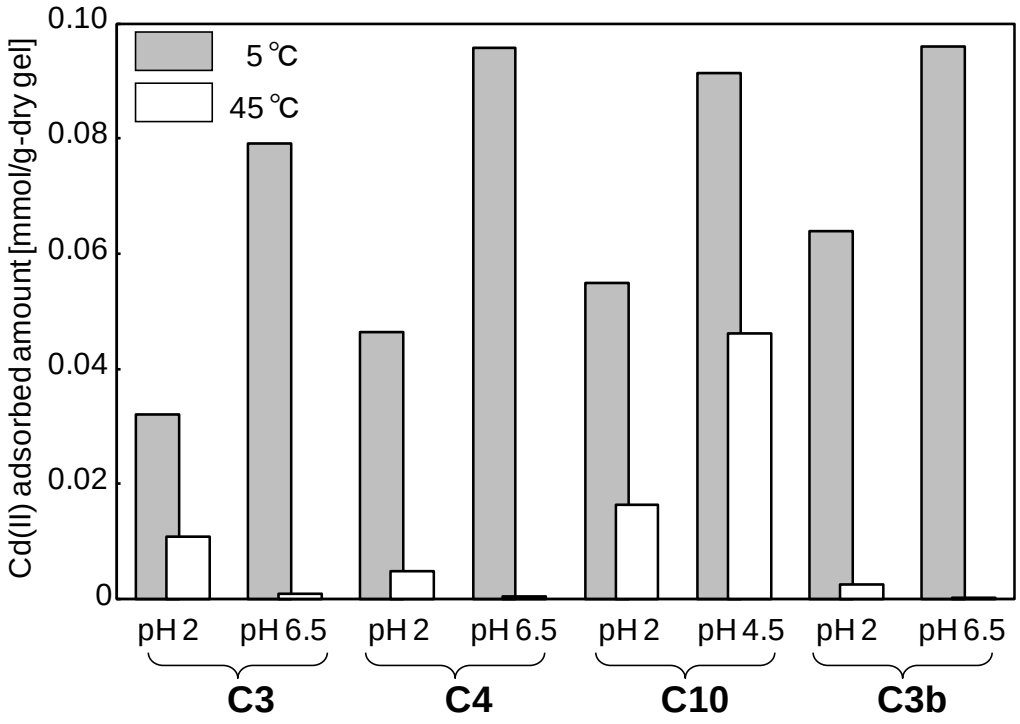


Figure 3. Thermo-responsive extraction of poly(TPEN-NIPA) gels at 5 ºC and 45 ºC.

Conclusion

In summary, we have synthesized TPEN derivatives bearing different side-chains involving the chain length and the branched structures and the prepared derivatives were subjected to the formation of poly(TPEN-NIPA) gels. The temperature-dependent change of extraction behaviors of cadmium(II) ion with poly(TPEN-NIPA) gels were highly influenced to the side-chain structures. The excellent thermo-responsive change particularly under highly acidic conditions such as pH=ca. 2 would be potentially practical for the chromatographic separation of metal ions, namely thermal swing chlormatography, which would be applied for the separation of minor actinides from high level radioactive wastes (HLW). The high performance of TPEN-NIPA gel **C3b** is remarkably noteworthy.

Acknowledgment

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Technology supported by MEXT for the measurement of high resolution mass spectra.

IV-5 Experimental

IV-5-1 General

General. NMR (500 MHz for ^{1}H, 125 MHz for ^{13}C) spectra were recorded on a Bruker Avance 500 spectrometer at the Center for Supports to Research and Education Activities, Kobe University. Chemical shifts are expressed in ppm using tetramethylsilane as an internal standard (0 ppm). Coupling constants (*J*) were shown in Hertz (Hz). IR (ATR) spectra were measured with Brucker Optics Alpha with Ge. TLC analyses were performed on analytical TLC plates coated with 60 F_{254} (E. Merck) silica gel or alumina on aluminum foil. Column chromatography was performed using silica gel Wakogel C200 (Wako Chemicals Co. Ltd.) or basic alumina (Wako Chemicals Co. Ltd or Merck). High-resolution mass spectra were measured at Nara Institute of Science and Technology with JEOL JMS-700. ICP-AES analysis was carried out with SII SPS3100 at the Center for Supports to Research and Education Acitivities of Kobe University.

Chemicals were purchased and used without further purification.

Chloromethylpyridine derivatives were prepared in a manner described previously. These spectroscopic characteristics and physical properties are shown below:

2-Chloromethyl-4-(buta-3-en-1-yloxy)pyridine (6b): ^{1}H NMR ($CDCl_3$) δ 8.35 (d, J = 5.8, 1H), 6.98 (d, J = 2.4, 1H), 6.72 (dd, J = 5.8, 2.4, 1H), 5.81-5.91 (m, 1H), 5.10-5.19 (m, 2H), 4.60 (s, 2H), 4.07 (t, J = 6.7, 2H), 2.52-2.57 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 165.87, 158.03, 150.43, 133.54, 117.58, 109.50, 109.24, 67.25, 46.54, 33.11; IR 1595, 1568, 1308, 1295, 1034, 991, 919 cm^{-1}; HRMS (EI+) calcd for $C_{10}H_{12}ClNO$ $[M]^+$; 197.0607; found: 197.0604.

2-Chloromethyl-4-(deca-9-en-1-yloxy)pyridine (6c): ^{1}H NMR ($CDCl_3$) δ 8.35 (d, J = 5.8, 1H), 6.97 (d, J = 2.4, 1H), 6.72 (dd, J = 5.8, 2.4, 1H), 5.80 (ddt, J = 17.2, 10.1, 6.7, 1H), 4.99 (dd, J = 17.2, 1.7, 1H), 4.93 (dd, J = 10.1, 1.0, 1H), 4.61 (s, 2H), 4.01 (t, J = 6.6, 2H), 2.04 (dt, J = 6.7, 6.6, 2H), 1.79 (quin, J = 6.6, 2H), 1.31-1.48 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 165.93, 157.99, 150.47, 138.94, 114.07, 109.39, 109.11, 68.00, 46.64, 33.63, 29.21, 29.10, 28.88, 28.75, 28.72, 25.76; IR 2925, 2854, 1596, 1568, 1467, 1308, 1296, 1025, 992, 909 cm^{-1}; HRMS (EI+) calcd for $C_{16}H_{24}ClNO$ $[M]^+$; 281.1546; found: 281.1541.

2-Chloromethyl-4-(2-methylprop-2-en-1-yloxy)pyridine (6d): ^{1}H NMR ($CDCl_3$) δ 8.37 (d, J = 5.9, 1H), 7.01 (d, J = 2.2, 1H), 6.75 (dd, J = 5.9, 2.2, 1H), 5.08 (s, 1H), 5.03 (s, 1H), 4.61 (s, 2H), 4.49 (s, 2H), 1.82 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.71, 158.15, 150.61, 139.48, 113.70, 109.73, 109.47, 71.64, 46.68, 19.27; IR 1594, 1568, 1478, 1311, 1241, 1177, 1018, 903 cm^{-1}; HRMS (EI+) calcd for $C_{10}H_{12}ClNO$ $[M]^+$; 197.0607; found: 197.0607.

***N,N,N',N'*-Tetrakis[4-(buta-3-en-1-yloxy)pyridin-2-ylmethyl]ethylenediamine (1b):** To a 25 mL of round-bottom flask were added compound **6b** (395.3 mg, 2.0 mmol), hexadecyltrimethylammonium chloride (3.2 mg, 0.01 mmol) and ethylenediamine (33.6 μL, 0.5 mmol) in H_2O (0.2 mL) under a nitrogen atmosphere. 5 M NaOH aq. (0.5 mL, 2.5 mmol) was added, and the resulting mixture was stirred vigorously at room temperature for 72 h. The reaction mixture was extracted with CH_2Cl_2 and the extract was washed with water, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on aluminum oxide (EtOAc:MeOH 100:0–10:1) to afford **1b** as pale brown oil in 64% yield. ^{1}H NMR ($CDCl_3$) δ 8.24 (d, J = 5.8, 4H), 6.98 (d, J = 2.4, 4H), 6.60 (dd, J = 5.8, 2.4, 4H), 5.76-5.89 (m, 4H), 5.07-5.16 (m, 8H), 4.60 (s, 2H), 3.94 (t, J = 6.6, 8H), 3.72 (s, 8H), 2.77

(s, 4H), 2.45-2.52 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 165.62, 161.72, 150.19, 133.95, 117.57, 109.14, 108.61, 67.05, 60.88, 52.63, 33.39; IR 1595, 1567, 1305, 1033, 993, 918, 829 cm^{-1}; HRMS (EI+) calcd for $C_{42}H_{52}N_6O_4$ $[M]^+$; 704.4050; found: 704.4051.

***N,N,N',N'*-Tetrakis[4-(deca-9-en-1-yloxy)pyridin-2-ylmethyl]ethylenediamine (1c):** To a solution of ethylenediamine (4.20 μL, 0.063 mmol) in THF/toluene (1:1, 0.5 mL) were successively added **6c** (71.5 mg, 0.25 mmol), potassium carbonate (35.1 mg, 0.254 mmol) and NaI (19 mg, 0.127 mmol) under nitrogen atmosphere. The reaction mixture was stirred for 19 h at 50 ˚C. The suspension was filtered through a Celite pad. The filtrate was evaporated, and the resulting oil was purified by chromatography on alumina (EtOAc:MeOH 100:0–20:1) to afford **1c** (49.5 mg, 76%) as a pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 8.23 (d, J = 5.8, 4H), 6.98 (d, J = 2.4, 4H), 6.59 (dd, J = 5.8, 2.4, 4H), 5.78 (ddt, J = 17.2, 10.1, 6.7, 4H), 4.96 (dd, J = 17.2, 1.7, 4H), 4.90 (dd, J = 10.1, 1.0, 4H), 3.87 (t, J = 6.6, 8H), 3.72 (s, 8H) 2.79 (s, 8H), 2.04 (dt, J = 6.7, 6.6, 8H), 1.72 (quin, J = 6.6, 8H), 1.29-1.40 (m, 40H); ^{13}C NMR ($CDCl_3$) δ 165.83, 160.94, 149.74, 139.02, 114.14, 109.11, 108.69, 67.88, 60.32, 52.27, 33.71, 29.34, 29.28, 29.00, 28.91, 28.85, 25.90; IR 2925, 2853,

1594, 1567, 1467, 1305, 1024, 993, 908 cm^{-1}; HRMS (FAB+) calcd for $C_{66}H_{100}N_6O_4$ $[M+H]^+$; 1041.7884; found: 1041.7894.

***N,N,N',N'*-Tetrakis[4-(2-methylprop-2-en-1-yloxy)pyridin-2-ylmethyl]ethyl enediamine (1d):** To a solution of ethylenediamine (4.02 μL, 0.06 mmol) in THF (0.482 mL) were successively added **6d** (47.1 mg, 0.241 mmol), potassium carbonate (33.3 mg, 0.24 mmol), *N*-hexadecyltrimethylammonium chloride (7.7 mg) and NaI (18.1 mg, 0.1 mmol) under nitrogen atmosphere. The reaction mixture was stirred for 22 h at 50 ˚C. The suspension was filtered through a Celite pad. The filtrate was evaporated, and the resulting oil was purified by chromatography on alumina (EtOAc) to afford **1d** (29.5 mg, 70%) as a pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 8.37 (d, J = 5.9, 1H), 7.01 (d, J = 2.2, 1H), 6.75 (dd, J = 5.9, 2.2, 1H), 5.08 (s, 1H), 5.03 (s, 1H), 4.61 (s, 2H), 4.49 (s, 2H), 1.82 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.12, 161.42, 149.85, 139.54, 113.14, 108.89, 108.53, 71.06, 60.58, 52.36, 19.05; IR 1593, 1567, 1481, 1307, 1241, 1166, 1019, 903, 748 cm^{-1}; HRMS (EI+) calcd for $C_{42}H_{52}N_6O_4$ $[M]^+$; 704.4050; found: 704.4044.

General Procedure for radical polymerization of NIPA with TPEN derivatives: To a 25 mL of sealed tube equipped with a magnetic stirring bar were added *N*-isopropylacrylamide (170 mg, 1.5 mmol) and TPEN derivative (0.019 mmol). The mixture was dissolved in 0.13 mL of DMF and AIBN (1.25 mol% or 2.50 mol%) was added in one portion. The resulting mixture was heated at 60 °C for 18 h. Then, the mixture was cooled to room temperature and washed with water repeatedly. Water was removed under reduced pressure at 50 °C to leave a colorless solid. Poly(TPEN-NIPA) gels (**C3**, **C4**, **C10** and **C3b**. see scheme 2) obtained were found to swell at room temperature in water and shrinking was observed when the mixture was heated to 45 °C.

Extraction of cadmium(II) ion with poly(TPEN-NIPA) gel: A 1 mM of aqueous $Cd(NO_3)_2$ solution was prepared. The pH value of the solution was controlled to 1.9, 2.0, 5.3, 5.9 by the addition of 1 M of aq. NH_4NO_3 and 1 M of HNO_3. Poly(TPEN-NIPA) gel (2.5 mol% of TPEN contents), whose concentration of the TPEN moiety was controlled to be 1.5 μmol, was added to 0.75 mL of the aqueous solution. Vigorous stirring of the mixture was continued for 60 min at 0 °C or 45 °C. An aliquot of the solution (0.2 mL) was

taken, passed thoruogh a membrane filter (0.2 μm), and diluted with distilled water to 4 mL, which was subjected to ICP-AES analysis. Cd^{2+} absorbed amount of poly(TPEN-NIPA) dry gel (mmol/g-dry gel) were summarized in Table 1.

Table 1. Extraction of Cd^{2+} by TPEN derivatives with chloroform.

poly(TPEN-NIPA) gel	Weight of dry-gel [mg]	Temp.	pH (before extraction)	pH (after extraction)	Cd absorbed amount [mmol/g-dry gel]
C3	7.8	5 °C	1.9	2.3	3.20×10^{-2}
			5.3	6.3	7.91×10^{-2}
		45 °C	2.0	2.5	1.07×10^{-2}
			5.9	6.7	0.08×10^{-2}
C4	7.8	5 °C	1.9	2.3	4.64×10^{-2}
			5.3	6.3	9.57×10^{-2}
		45 °C	2.0	2.4	0.48×10^{-2}
			5.9	6.5	0.04×10^{-2}
C10	8.4	5 °C	1.9	2.3	5.50×10^{-2}
			5.3	4.3	9.13×10^{-2}
		45 °C	2.0	2.4	1.64×10^{-2}
			5.9	4.9	4.62×10^{-2}
C3b	7.8	5 °C	1.9	2.5	6.40×10^{-2}
			5.3	6.5	9.60×10^{-2}
		45 °C	2.0	2.3	0.26×10^{-2}
			5.9	6.7	0.01×10^{-2}

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Chapter IV

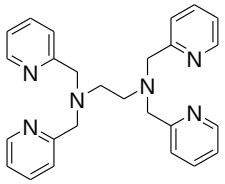
Temperature-dependent Change of Extraction Performance of Soft Cadmium(II) Ion with TPEN-NIPA gel. Studies on the Effect of Ethylenediamine Skeleton

Abstract: TPEN (*N*,*N*,*N*′,*N*′-tetrakis(2-pyridylmethyl)ethylenediamine) derivatives of different skeleton of the ethylene moiety are designed and synthesized. The obtained product is subjected to radical copolymerization with *N*-isopropylacrylamide (NIPA) to afford the polymer gel. Temperature-dependent extraction performance of TPEN derivatives and the corresponding polymer gels is compared at different temperatures and pH values.

IV-1 Introduction

We have recently shown that TPEN-(poly-NIPA) gel exhibits thermo-responsive extraction of soft metal ions. TPEN-NIPA gel was prepared by the copolymerization of *N*-isopropylacrylamide (NIPA) and TPEN (*N,N,N',N'*-tetrakis(2-pyridylmethyl)ethylenediamine) derivatives bearing a polymerizable double bond on the subsituent of the pyridine ring.[1] TPEN, which is a hexadentate ligand bearing six nitrogen donors, efficiently extracts several soft metal ions and is recognized as a possible candidate for the separation of minor actinides (MA) such as Am and Cm from high-level waste during the reprocessing of the nuclear fuel of fast breeder reactor.[2-4] Since poly-NIPA gel shows thermo-responsive reversible swelling/shrinking change at the LCST, extraction performance of the TPEN-NIPA gel, in which the TPEN derivatives are employed as a cross-linker, has shown to change depending on the temperature.[5] Concerning the relationship of the TPEN structure toward the extraction performance, we have studied the effect of the number of polymerizable double bond,[6] chain length of the spacer between double bond and the pyridine ring[7] and branched structure on the spacer.[8] It is also intriguing to study the effect of the structure of

ethylenediamine moiety. We herein report synthesis of several TPEN derivatives with different diamine structure, radical copolymerization of thus prepared TPEN derivatives and NIPA, and studies on the temperature-dependent extraction of cadmium(II) ion with thus obtained TPEN-NIPA gel derivatives.



TPEN

IV-2 Results and Discussion

TPEN derivatives we have designed are ethylenediamine (**1**), 1,3-propanediamine (**2**), and 1,5-diamino-3-oxapentane (**3**), whose amino group is substituted with 2-chloromethylpyridine bearing a 2-methyl-2-propenyloxy substituent at the 4-position of the pyridine ring. Synthesis of **1-3** was carried out in a similar manner to that of TPEN (**1**). NIPA gels composed of **1-3** as a cross linker were prepared by radical polymerization with AIBN as an initiator in the presence of 2.5 mol% of **1-3** to give the corresponding gel compound in good yields. The obtained gels showed thermo-responsive swelling and shrinking around 30-35 °C. The volume change between swelling and shrinking of **1-3** was found to be 3.7,

3.6, and 3.8, respectively. Attempted spectroscopic characterization of gels **1-3** were unsuccessful. Since the obtained gels were completely insoluble in any solvents, it is difficult to characterize structure of the cross linker by NMR analyses. It was also unsuccessful to observe characteristic absorptions of pyridine rings in IR spectra due to their insufficient amount to be detected.

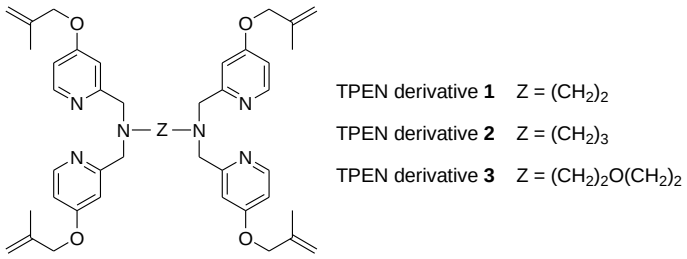


Figure 1. Structure of TPEN derivatives **1-3**.

Extraction performance of TPEN gels composed of **1-3** was examined with 1 mM solutions of $Cd(NO_3)_2$, whose pH was controlled to 2.0 or 5.0. The polymer gel was added to the aqueous cadmium solution and stirring was continued for 1 h at 5 °C and 40 °C, respectively. Liquid-liquid extraction was also carried out with **1-3** using 1 mM solution of chloroform, at 5 °C and 40 °C at pH = 2. Table 1 shows the results on the liquid-liquid extraction performance of TPEN derivative **3**, which possesses $(CH_2)_2O(CH_2)_2$ moiety instead of ethylene diamine. Excellent extraction performance was observed

similarly to that of TPEN. It was also found that the performance was irrespective of the extraction temperature to observe mostly similar %extraction values at pH=5.0. Although the performance was slightly inferior at pH=2.0, Cd^{2+} ion was similarly extracted at both temperatures.

Table 1. Extraction of Cd^{2+} with TPEN derivatives of **3** at 5 °C and 40 °C at pH = 2 and pH = 5.[a]

	%Extraction			
	pH = 2		pH = 5	
TPEN derivative	5 °C	40 °C	5 °C	40 °C
3	55.7	57.5	89.8	87.2

[a] Concentration of the cadmium ion was estimated by ICP-AES analysis in the aqueous phase.

By contrast to the above results on the liquid-liquid extraction, temperature-dependent extraction performance was observed in the extraction with TPEN-NIPA polymer gels **1-3**. Extraction was performed with 1 mM solutions of $Cd(NO_3)_2$, whose pH was controlled to 2.0 or 5.0, and TPEN-NIPA gels **1-3** at 5 °C and 40 °C, respectively. As summarized in Table 2, extraction with **1** at pH of 5.0 showed that 85.0% of cadmium was

incorporated in the polymer gel at 5 °C, while the performance was decreased to 11.1% when the temperature was raised to 40 °C. Worthy of note is that such a temperature-dependent change was observed in the extraction at pH of 2.0 although the %extraction values were slightly inferior to those at pH =5. Extraction with other polymer gels **2-3** also showed similar performance to that with **1**.

Table 2. Extraction of Cd^{2+} with NIPA gels composed of **1-3** at 5 °C and 40 °C at pH = 2 and pH = 5.

TPEN-NIPA gel	%Extraction			
	pH = 2		pH = 5	
	5 °C	40 °C	5 °C	40 °C
gel **1**	47.9	18.2	85.0	11.1
gel **2**	28.2	2.4	85.0	26.4
gel **3**	23.0	10.5	79.3	7.1

The results showed that different chain length in the ethylenediamine moiety of TPEN did not influence the extraction performance suggesting that all of six nitrogen atoms of TPEN are not crucial for the incorporation of a metal ion. Subsequently, chelation with two

nitrogen atoms of ethylenediamine leading to tight five-membered ring structure involving the cadmium atom is not the prerequisite for the efficient extraction.

If the five-membered chelation with ethylenediamine moiety is not crucial for the extraction of cadmium ion, independent tridentate chelation with bis(2-pyridylmethyl)amino moiety is an alternative chelating structure, which may allow 1:2 complexation in **1-3**. Measurement of ^{1}H NMR spectrum in the mixture of **3** and a cadmium ion was thus carried out. Figure 2 shows the spectra of the different ratio of **3** and $Cd(NO_3)_2$. The mixture of **3** and 0.5 equiv of $Cd(NO_3)_2$ (**b**) indicated that several new signals that suggested formation of a metal complex were observed accompanied by characteristic signals, which were identical to those shown in (**a**). The 1:1 mixture of **3** and $Cd(NO_3)_2$ (**c**) was completely identical to the new signals of (**b**). However, the NMR spectrum in the further addition of $Cd(NO_3)_2$ (1:10) also showed similar signals to (**c**). These results suggest that complexation of $Cd(NO_3)_2$ with **3** forms the 1:1 adduct.

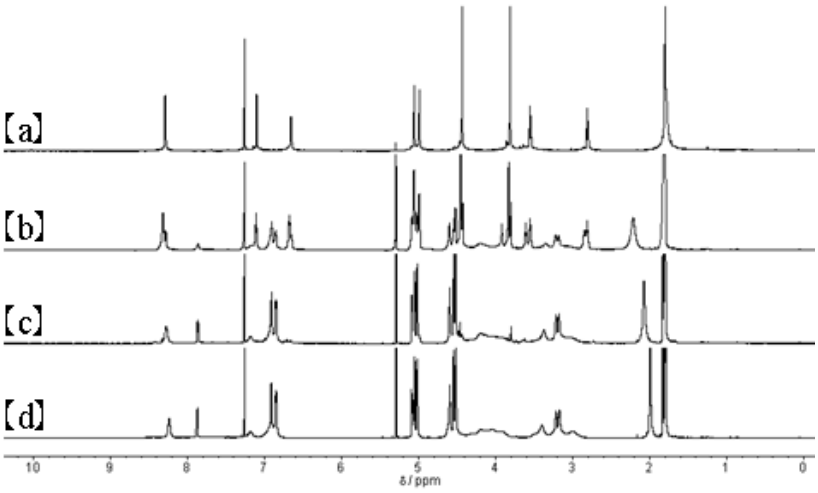


Figure 2. NMR spectra of uncomplexed **3(a)** and the mixture of **3** and Cd^{2+} (**b-d**). (**b**)1:0.5 (**c**)1: 1 (**d**)1:10 .

IV-3 Conclusion

In conclusion, several TEPN derivatives bearing the different number of spacer atoms from ethylenediamine are designed and synthesized. Extraction performance of these derivatives **1-3** and the corresponding polymer gels that are obtained by the radical copolymerization of **1-3** and NIPA was studied to reveal that the spacer structure was irrespective of the extraction of the cadmium ion in polymer gels as well as liquid-liquid system. Polymer gels of **1-3** showed temperature-dependent swelling and shrinking and thus induced change of the extraction performance, which was also irrespective of the spacer structures. These results suggest that the

performance is not significantly influenced by the difference of the spacer structure, while all of these extractants forms 1:1 chelation with cadmium.

IV-4 Experimental

General. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were measured in $CDCl_3$ with Brucker Avance 500. Chemical shifts are expressed in ppm using $CHCl_3$ (7.24 ppm) for ^{1}H NMR and the central signal of $CDCl_3$ (77 ppm) for ^{13}C NMR as internal standards. Coupling constants (J) were shown in Hertz (Hz). IR (ATR) spectra were measured with Brucker Optics Alpha with Ge. High-resolution mass spectra were measured at Nara Institute of Science and Technology with JEOL JMS-700. ICP-AES analysis was carried out with SII SPS3100. Column chromatography was performed using silica gel (Wakogel C200, Wako Chemicals Co. Ltd.) or basic alumina (Wako Chemicals Co. Ltd or Merck).

Syntheses of 1-3. TPEN derivatives with a different spacer structure were prepared in a manner similar to those reported previously.

***N,N,N',N'*-Tetrakis[4-(2-methyl-2-propenyloxy)-2-pyridylmethyl]-ethylen ediamine (1)**

To a solution of ethylenediamine (26.1 μL, 0.39 mmol) in acetonitrile (3.12 mL) were successively added 4-methallyloxy-2-(chloromethyl)pyridine (0.309 g, 1.56 mmol), K_2CO_3 (0.431 mg, 3.12 mmol) and NaI (0.117g, 0.708 mmol). The reaction mixture was stirred for 8 h at 80 °C. The suspension was filtered through a Celite pad. The filtrate was evaporated, and the resulting residue was purified by chromatography on aluminum oxide (chloroform/methanol = 30:1) to afford *N,N,N',N'*-Tetrakis[4-(2-methyl-2-propenyloxy)-2-pyridylmethyl]-ethylenediamine as a brown oil. ^{1}H NMR: δ 8.27 (d, *J*=5.75 Hz, 4H), 7.03 (d, *J*=2.45 Hz, 4H), 6.60 (dd, *J*=2.50, 5.65 Hz, 4H), 5.01 (d, *J*=29.5 Hz, 12H), 4.39 (s, 8H), 2.79 (s, 4H), 1.79 (s, 12H). ^{13}C NMR: δ 5.1, 6.8, 38.3, 46.1, 57.3, 95.0, 99.2, 125.6, 135.8, 151.2, 162.6. IR: 2943, 1595, 1309, 1052 cm^{-1}. HRMS (EI) found: 704.4044, Calcd for $C_{42}H_{52}N_6O_4$: 704.4050.

_N,N,N',N'_-Tetrakis[4-(2-methyl-2-propenyloxy)-2-pyridylmethyl]-1,3-propanediamine (2)

^{1}H NMR: δ 8.27 (d, *J*=5.75 Hz, 4H), 7.03 (d, *J*=2.45 Hz, 4H), 6.64 (dd, *J*=2.55, 5.70 Hz, 4H), 5.30 (s, 2H), 5.02 (d, *J*=32.15 Hz, 8H), 3.72 (s, 8H), 2.59 (s, 4H), 1.80 (s, 12H). ^{13}C NMR: δ 5.2, 10.8, 38.7, 46.3, 57.2, 94.7, 94.9, 99.3,

125.7, 136.0, 147.7, 151.3. IR: 1020, 1308, 1594, 2940 cm^{-1}. HRMS (EI) found: 718.4207, Calcd for $C_{43}H_{54}N_6O_4$: 718.4207.

***N,N,N',N'*-Tetrakis[4-(2-methyl-2-propenyloxy)-2-pyridylmethyl]-1,5-diamino-3-oxapentane(3)**

^1H NMR: δ 8.29 (d, *J*=5.70 Hz, 4H), 7.10 (d, *J*=2.35 Hz, 4H), 6.65 (dd, *J*=2.45, 7.95 Hz, 4H), 5.02 (d, *J*=33.8 Hz, 8H), 4.43 (s, 8H), 3.81 (s, 8H), 3.55 (s, 4H), 2.81 (s, 4H), 1.80 (s, 12H). ^{13}C NMR: δ 5.1, 39.8, 46.7, 55.3, 57.2, 94.80, 94.8, 99.2, 125.6, 135.8, 147.5, 151.2. IR: 1020, 1308, 1594, 2942 cm^{-1}. HRMS (EI) found: 748.4318, Calcd for $C_{44}H_{56}N_6O_5$: 748.4318.

Radical polymerization of NIPA with TPEN derivatives

poly-NIPA gels with 2.5 mol% of TPEN were synthesized in a similar manner described previously.[6] The obtained TPEN-NIPA gels were hardly soluble in organic solvents and water and showed swelling/shrinking change at 35 °C.

Extraction of cadmium(II) ion with TPEN-NIPA gel

A 1 mM of aqueous $Cd(NO_3)_2$ solution was prepared. The pH value of the solution was controlled to 2.1 and 5.3 by the addition of 1M of aq NH_4NO_3 and 1 M of HNO_3. TPEN-NIPA gel (2.5 mol% of TPEN contents), whose

concentration of the TPEN moiety was controlled to be 1.5μmol, was added to 0.75mL of the aqueous solution. Vigorous stirring of the mixture was continued for 60 min at 5 °C or 45 °C. An aliquot of the solution was taken, passed through a membrane filter (0.2 μm), and 0.2 mL of the filtrate was diluted with distilled water to 4 mL, which was subjected to ICP-AES analysis. The percent extraction value was calculated as

$\%E = 100 \cdot D/(D+1)$, $\{D = ([Cd^{2+}]_{ini} \cdot [Cd^{2+}])/[Cd^{2+}]\}$

$[Cd^{2+}]_{ini}$: concentration of Cd^{2+} in water before extraction;

$[Cd^{2+}]$: concentration of Cd^{2+} in water after extraction.

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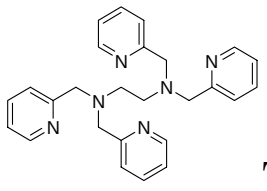
Chapter V

Synthesis of TPEN Derivatives bearing a Fluoroalkyl Substituetnt and Its Extraction Behavior of Soft Metal Ion

Abstract: *N,N,N',N'*-tetrakis(2-pyridylmethyl)ethylenediamine (TPEN) derivatives bearing a fluoroalkyl substituent are synthesized and employed for the soft metal extraction. The extraction behaviors of Cd^{2+} from aqueous solutions into chloroform and fluorous solvent are investigated with the synthesized TPEN derivatives as a ligand. The extraction performance of TPEN derivatives is found to be enhanced by the introduction fluoroalkyl group to reveal that TPEN derivatives bearing tetrafuluoro and pentafluoroalkyl group show excellent extraction performance at ca. pH=1, while TPEN with a longer fluoroalkyl chain shows inferior extraction. It is also found that TPEN derivatives bearing fluoroalkyl group are employed for the extraction of cadmium ion with a fluorous solvent system composed of HFE7100/$H(CF_2)_2CH_2OH$ (10:1). NMR studies reveals that TPEN with cadmium forms the 1:1 complex.

V-1 Introduction

Solvent extraction is known to be a very effective and selective separation method for metal ions. Numerous studies have been performed to develop efficient separation and concentration processes of metals with a solvent extraction technique, which is well known to be one of the promising techniques to separate and concentrate metals on an industrial scale. The extractant is known to have crucial effect on the separation and extraction efficiency in the solvent extraction process. Therefore, it is very important to develop an efficitent extractant for a target metal ion. The design of the complexing agents plays an important role in such processes. In the solvent extraction of metal ions it is now established that a variety of ligand types can be employed as the extracting agent and, for example, can form chelate or solvated complexes with metal ions. In particular, TPEN type ligands plays an important role in the separation from waste water.



TPEN

In our preliminary communication, we have shown that TPEN derivatives bearing alkoxy groups improved extraction performance of Cd^{2+}

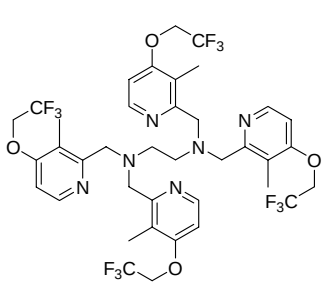
from acidic aqueous solution. However, the acid tolerance of the hydrophobic TPEN was found to be far from satisfactory and we recognized that further improvement of hydrophobic characteristics of TPEN derivatives with molecular design based an organic synthesis is necessary.

On the other hand, fluorocarbons attract much interest in a wide range of fields in organic chemistry, biochemistry and material science. A number of organic molecules as well as polymer materials are shown to change their performance by the introduction of fluorine-substituted organic groups into the core structure. In particular, remarkably low intermolecular interaction of fluorine-containing molecules induces highly hydrophobic and fluorophilic characteristics. Accordingly, introduction of fluoroalkyl substituents onto TPEN derivatives is intriguing for the development of a practical extraction of metal ions. In the present study, we report synthesis and properities of designer TPEN derivatives bearing fluoroalkyl substituent at the 4-position of the pyridine ring are synthesized and extraction ability of Cd^{2+} with TPEN derivatives are studied. In particular, we focused on the fluorocarbons effect of TPEN type ligand and the extraction ability of metal ions.

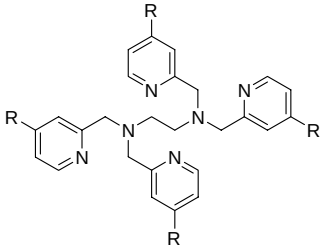
V-2 Results and Discussion

Synthesis of TPEN derivatives

Chart 1 illustrates structure of TPEN derivatives bearing a fluoroalkyl substitutent at the 4-position of pyridine ring. The substituent is connected to the pyridine ring as ether bearing methylene unit as a spacer toward the fluoroalkyl group.The electronic effect of the electronegative fluoroalkyl group would thus be canceled by the introduction of the methylene spacer. There would be little difference of the extraction performance of the TPEN derivatives **9a** from TPEN **9f** albeit improved hydrophobic characteristics by the introduction of fluorine atoms.



F3TPEN (**9a**)



F4TPEN (**9b**) R = $OCH_2CF_2CF_2H$
F5TPEN (**9c**) R = $OCH_2CF_2CF_3$
F7TPEN (**9d**) R = $OCH_2CF_2CF_2CF_3$
F8TPEN (**9e**) R = $OCH_2CF_2CF_2CF_2CF_2H$
F20TPEN (**9f**) R = $OCH_2(CF_2)_9CF_2H$

Chart 1 Chemical structure of TPEN derivatives bearing fluoroalkyl substituent.

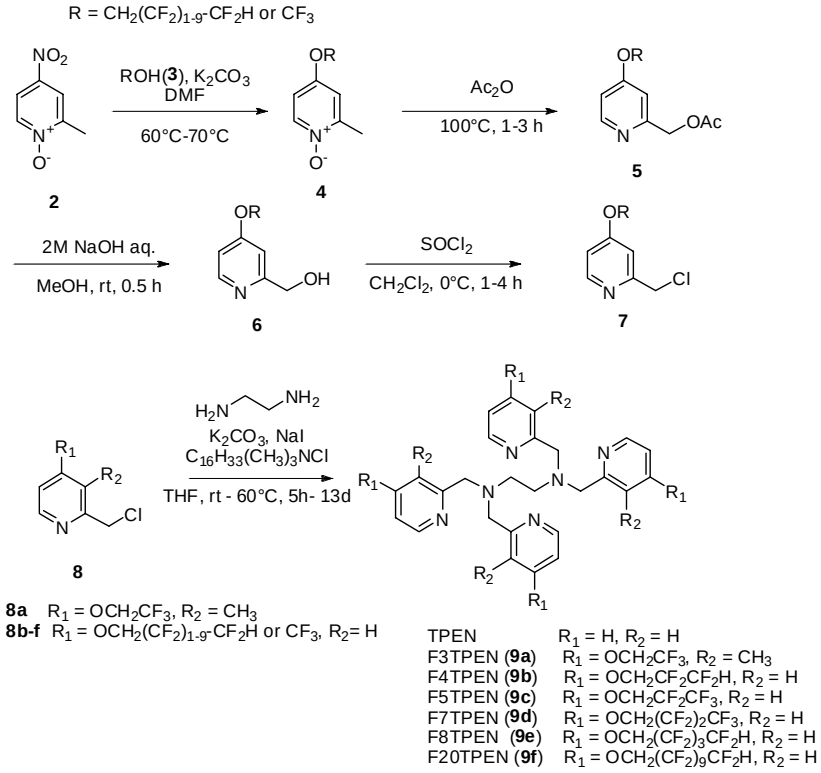
The synthetic procedure for the TPEN derivatives bearing a fluoroalkyl substituent on the pyridine ring is summarized in Scheme 1. Synthesis was performed in a similar manner to that of TPEN derivatives bearing an alkoxy substituent on the pyridine ring. The reaction of

2-methyl-4-nitropyridine 1-oxide with fluorinated primary alcohols **3** in the presence of potassium carbonate in DMF gave the corresponding **4** in 53-89% yield. The reaction of ROH bearing CH_2 spacer proceeded smoothly compared with that by 1-octanol. The reaction took place under mild conditions to afford the corresponding ethers in good yields. The obtained 4-fluoroalkoxy-2-(hydroxymethyl)pyridine *N*-oxides **4** were subjected to the reaction with acetic anhydride to give 2-acetoxy derivatives **5**. Hydrolysis of the acetoxy group was carried out by sodium hydroxide in methanol at room temperature. The hydroxyl group of 2-(hydroxymethyl)pyridines **6** were chlorinated with thionyl chloride in dichloromethane at 0 ºC to afford chloromethylpyridines **8b-f** in reasonable yields. On the other hand, **8a** (R1=OCH_2CF_3; R2=CH_3) was commercially available as a hydrochloride salt. The reaction of 1,2-ethylenediamine with 4 equivalents of chloromethyl pyridine derivatives **8** was performed in the presence of K_2CO_3 (4.0 or 8.0 eq.) and $C_{16}H_{33}(CH_3)NCl$ (10.0 mol%) at room temperature to 60 ºC in THF to afford fluorinated TPEN derivatives **9** in 35-78% yields.[3]

Synthesized TPEN derivatives bearing a fluoroalkyl substituent was found to be dissolved in various organic solvents such as ethyl acetate and

chloroform, while gardly soluble in water. It is suggested that TPEN derivatives of hydrophobic property improved.

Measurement of C13NMR spectrum revealed that chemical shift of signals corresponding to the carbon atoms of pyridine ring exhibited little difference between TPEN derivatives bearing a fluoroalkyl substituent and TPEN derivatives bearing a alkoxy substituent. It suggests that the fluoroalkyl substituent hardly influence basicity of pyridine.



Scheme 1. Synthesis of TPEN derivatives bearing a fluoroalkyl substituent

Liquid-liquid extraction studies

With thus obtained TPEN derivatives bearing potentially hydrophobic fluoroalkyl substituents, the extraction performance was examined with cadmium ion, which was recognized as a class of soft metal and the extraction performance is relatively similar to minor actinides such as Am and Cm. The experiments were carried out with acidic aqueous solution and a solution of TPEN derivatives in Chloroform under different pH values. The liquid-liquid extraction was carried out with a phase ratio $V_{(W)}$: $V_{(org)}$ of 1:1. In the aqueous phase 1.0 mM nitric acid solution of $Cd(NO_3)_2$ and the pH was controlled by the addition of F3TPEN to F20TPEN derivative **9** was dissolved in chloroform, whose concentration was controlled to 1.0 mM. Both solution were added to a test tube and the mixture was vigorously shaken for 5 min. Then, the phases were separated, centrifuged. An aliquot of the aqueous phase was taken and subjected to ICP-AES[4] analysis to estimate the extracted amount of Cd^{2+}. The distribution ratio D_M for Cd^{2+} was calculated as follows:

$D_M = [Cd^{2+}]_{(org)} / [Cd^{2+}]_{(w)}$

The percent extraction value *E(%)*was estimated to be

$E(\%) = 100\ D_M / (D_M+1)$

Figure 1 summarizes the results of the %extraction values at various pH with chloroform by TPEN derivatives F3-F5TPEN. Amoug these, TPEN derivatives bearing pentafluoropropoxy substituents F5TPEN showed highest extraction performance at ca. pH1. Such high performance has not been achieved in other extractants as well as TPEN derivatives due to the excellent hydrophobicity of the fluoroalkyl group.

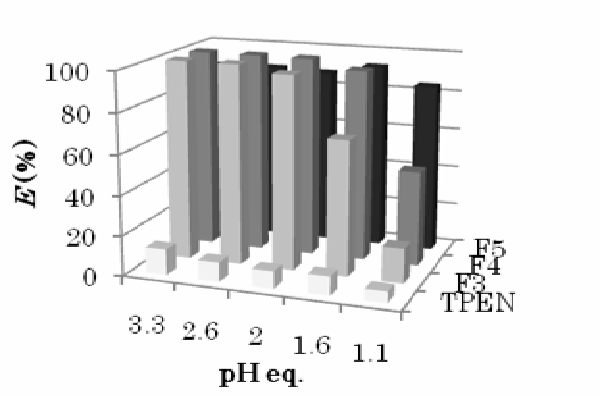


Figure 1. Extraction of Cd^{2+} ion by TPEN derivatives F3,F4,F5 with chloroform.

However, TPEN derivative with longer fluoroalkyl chain length F7-F20TPEN were found to show inferior extraction to F5TPEN (Figure 2). After the extracts of F7-F20TPEN derivatives, white solid extracted it to the verge of the aqueous phase and the organic facies. Therefore, the extraction declined performance was thought as a cause to the decrease of solubility to chloroform of F7-F20TPEN derivatives. Then, for the purpose of the

improvement of solubility we were examined to use fluorous solvent (HFE7100:$CF_2HCF_2CH_2OH$ = 10 : 1), and the extraction performance was evaluated.

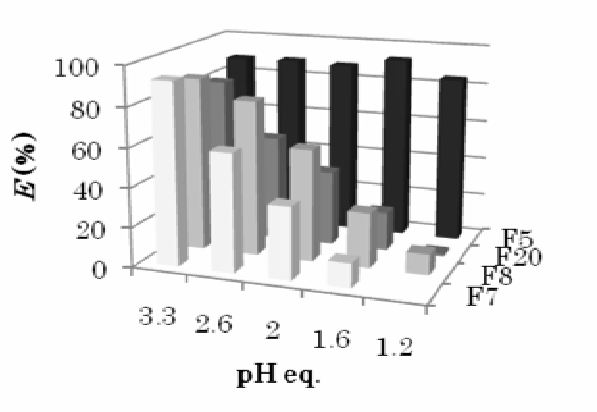


Figure 2. Extraction of Cd^{2+} ion by TPEN derivatives F7,F8,F20-with chloroform.

Figure 4. shows the results for extraction of Cd^{2+} from water into fluorous solvent (HFE7100:$CF_2HCF_2CH_2OH$ = 10 : 1).[5,6] F5TPEN demonstrated a high extraction performance as well as the case to use the chloroform solvent when the fluorous solvent was used. In addition, the extraction performance has improved in F8TPEN dramatically. As a result of having experimented on extraction like the case in which a chloroform solvent was used for about all TPEN derivatives extraction performance proved to be improved. The results clearly indicate that the fluorous solvent system is highly effective for **9** to extract Cd^{2+}.

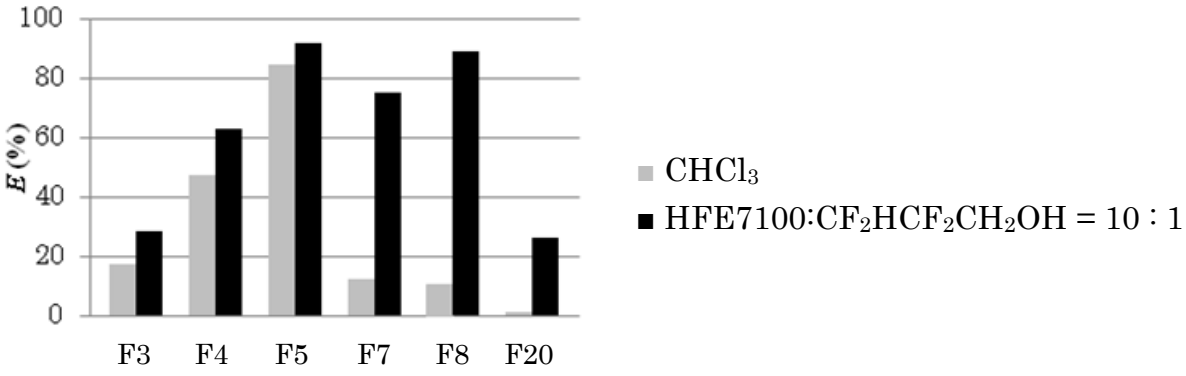


Figure 4. Extraction of Cd^{2+} ion by TPEN derivatives bearing fluoroalkyl substituents with fluorous solvent (HFE7100 / $H(CF_2)_2CH_2OH$) at pH 1.

NMR studies of Cd^{2+} complexes.

Measurement of 1H NMR spectrum in the mixture of F5TPEN and a Cd^{2+} was carried out. Figure 5 shows the spectra of the different ratio of F5TPEN and $Cd(NO_3)_2$. The mixture of F5TPEN and 0.5 equiv of $Cd(NO_3)_2$ (**b**) indicated that several new signals that suggested formation of a metal complex were identical to those shown in (**a**). The 1:1 mixture of F5TPEN and $Cd(NO_3)_2$ (**c**) was completely identical to the new signals of (**b**). However, the NMR spectrum in the further addition of $Cd(NO_3)_2$ (1:10) also showed similar signals to (**c**). These results suggest that complexation of $Cd(NO_3)_2$ with F5TPEN forms the 1:1 adduct.

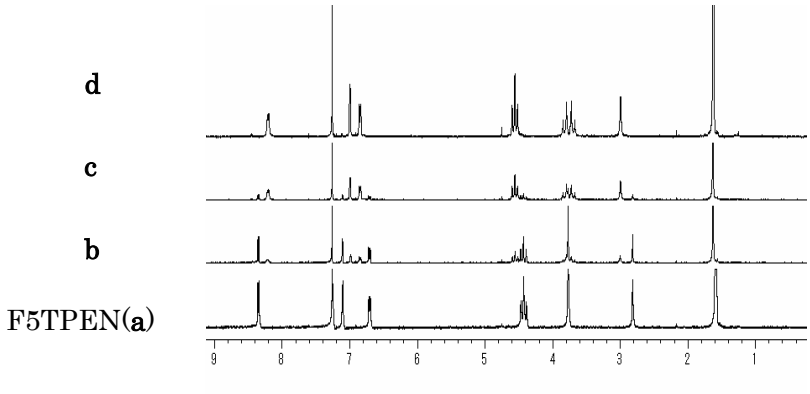


Figure 5. NMR spectra of uncomplexed F5TPEN (a)and the mixture of F5TPEN and Cd^{2+} (b-d). (b) 1:0.5, (c)1:1, (d)1:5.

V-3 Conclusion

In conclusion several TPEN derivatives bearing fluoroalkyl substituents are design and synthesized. the extraction performance of TPEN derivatives **9a-9f** was studied with chloroform and a flourous solvent system. The synthesized TEPN derivatives indicated excellent extraction performance particularly when the extraction was performed with highly acidic aqueous solutions of the cadmium ion. NMR studies concerning the chelation structure revealed that extractants forms 1:1 chelation with Cd^{2+}.

V-4 Experimental

General

NMR (500 MHz for ^{1}H, 125 MHz for ^{13}C) spectra were recorded on a Bruker Avance 500 spectrometer at the Center for Supports to Research and Education Activities, Kobe University or NMR (300 MHz for ^{1}H, 75 MHz for ^{13}C) spectra were recorded on Varian Gemini 300. Chemical shifts are expressed in ppm using chloroform as an internal standard (7.26 ppm), unless noted. Coupling constants (*J*) were shown in Hertz (Hz). IR (ATR) spectra were measured with Brucker Optics Alpha with Ge. TLC analyses were performed on analytical TLC plates coated with 60 F_{254} (E. Merck) silica gel or alumina on aluminum foil. Column chromatography was performed using silica gel Wakogel C200 (Wako Chemicals Co. Ltd.) or basic alumina (Wako Chemicals Co. Ltd or Merck). High-resolution mass spectra (EI or FAB or ESI) were measured at Nara Institute of Science and Technology with JEOL JMS-700. ICP analysis was carried out with SII SPS3100.

_N,N,N',N'_-Tetrakis((4-trifluoroethoxy-3-methylpyridine-2-yl)methyl) ethane-1,2-diamine (9a)

To a solution of ethane-1,2-diamine (70 μL, 1.04 mmol) in THF (2.0 mL) and H_2O (2.0 mL) were successively added 4-(2,2,2-trifluoroethoxy)-2-(chloromethyl)-3-methylpyridine hydrochloride (1.0 g, 4.2 mmol), sodium hydroxide (333 mg, 8.34 mmol), $[CH_3(CH_2)_{15}N(CH_3)_3]Cl$ (3.3 mg, 0.01 mmol) and KI (694 mg, 4.2 mmol) under nitrogen atmosphere. The reaction mixture was stirred for 87 h at room temperature. The suspension was filtered through a Celite pad. The filtrate was evaporated, and the resulting residue was purified by chromatography on alumina (ethyl acetate / methanol = 20 / 1) to afford _N,N,N',N'_-tetrakis((4-trifluoroethoxy-3-methylpyridine-2-yl)methyl)ethane-1 ,2-diamine (**3a**, 690 mg, 75%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 5.6 Hz, 4H), 6.57 (d, J = 5.6 Hz, 4H), 4.33 (q, J = 7.8 Hz, 8H), 3.64 (s, 8H), 2.63 (s, 4H), 1.91 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 147.2, 124.2, 122.7, 122.0, 105.6, 65.9, 65.6, 59.1, 52.0, 10.0; IR 1579, 158.3, 1259, 1165, 971, 860 cm^{-1}; mp 106.7-107.9 ˚C; HRMS (FAB+) calcd for $C_{38}H_{40}F_{12}N_6O_4$ $[M+H]^+$; 873.2998; found: 873.3005.

4-(2,2,3,3-Tetrafluoropropyloxy)-2-methylpyridine *N*-oxide (4b)[3d]

To a solution of 4-nitro-2-picoline *N*-oxide (1.54 g, 10 mmol) in DMF (10 mL) were added 2,2,3,3-tetrafluororo-1-propanol (1.62 mL, 18 mmol) and K_2CO_3 (4.14 g, 30 mmol) at 70 ˚C. The reaction mixture was stirred for 1 h. The suspension was filtered through a Celite pad and the filtrate was concentrated under reduced pressure to leave a crude oil, which was employed for the next reaction without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 7.2 Hz, 1H), 6.89 (d, J = 3.4 Hz, 1H), 6.81 (dd, J = 7.2, 3.4 Hz 1H), 6.11-5.88 (m, 1H), 4.41 (t, J = 11.9 Hz, 2H), 2.54 (s, 3H).

(4-(2,2,3,3-Tetrafluoropropoxy)pyridine-2-yl)methanol (6b) [3d]

A mixture of 4-(2,2,3,3-tetrafluoropropoxy)-2-methylpyridine *N*-oxide (2.71 g, 11.3 mmol), acetic anhydride (5.4 mL), and H_2SO_4 (10 μL) was stirred at 100 °C for 3 h. After cooling the resulting mixture to room temperature and following removal of acetic anhydride in vacuo, the residue was dissolved in a solution of sodium hydroxide (800 mg, 20 mmol) in methanol (11.0 mL) – H_2O (3.0 mL). The mixture was stirred at room temperature for 1 h. After removal of methanol, the residue was dissolved in 10 mL of CH_2Cl_2

and the solution washed with brine. The organic layer was dried over anhydrous sodium sulfate. Removal of the solvent left a crude oil, which was purified by column chromatography on silica gel using ethyl acetate as an eluent to afford 1.74 g of (4-(2,2,3,3-tetrafluoropropoxy)pyridine-2-yl)methanol (overall from 4-nitro-2-picoline *N*-oxide, 72%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, J = 5.8 Hz 1H), 6.90 (d, J = 2.3 Hz 2H), 6.80 (dd, J = 5.8, 2.5 Hz, 1H), 6.13-5.92 (m, 1H), 4.75 (s, 2H), 4.43 (t, J = 11.7 Hz, 2H), 3.75 (bs, 1H).

4-(2,2,3,3-Tetrafluoropropoxy)-2-(chloromethyl)pyridine (7b)

Thionyl chloride (0.32 mL, 4.40 mmol) was added to a solution of (4-(2,2,3,3- tetrafluoropropoxy)pyridin-2-yl)methanol (750 mg, 3.14 mmol) in 0.12 mL of CH_2Cl_2. The reaction mixture was stirred at 0 ºC for 1 h. After the reaction is complete, excess thionyl chloride was quenched by the addition of ^{i}PrOH (0.12 mL, 1.57 mmol). The resulting mixture was poured into sat. aqueous $NaHCO_3$ and then extracted with CH_2Cl_2. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to leave a crude oil, which was purified by column chromatography

on silica gel using ethyl acetate as an eluent to give 4-(2,2,3,3-tetrafluoropropoxy)-2-(chloromethyl)pyridine (717 mg, 88%) as a light brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (d, J = 5.7 Hz 1H), 6.98 (d, J = 2.2 Hz, 1H), 6.73 (dd, J = 5.6, 2.4, Hz, 1H), 6.11-5.88 (m, 1H), 4.56 (s, 2H), 4.36 (t, J = 11.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 158.8, 151.0, 116.4-106.8 (m), 64.7, 64.4, 64.2, 46.3; IR, 1597, 1315, 1106, 949, 836 cm^{-1}; HRMS (EI+) calcd for $C_9H_8ClF_4NO$ 257.0231; found: 257.0228.

N,N,N',N'-Tetrakis((4-(2,2,3,3-tetrafluoropropoxy)pyridine-2-yl) methyl)ethane-1,2-diamine (9b)

The reaction was carried out in a similar manner to the synthesis of **3a** with stirring at room temperature for 13 days to afford 50% of **3b** as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, J = 5.7 Hz 4H), 7.09 (d, J = 2.3 Hz, 4H), 6.68 (dd, J = 5.6, 2.5, Hz, 4H), 5.99 (m, 4H), 4.34 (t, J = 11.8 Hz, 8H), 3.77 (s, 8H), 2.82 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.0, 161.8, 150.7, 116.6-106.9 (m), 64.7, 64.4, 64.2, 60.4, 52.1; IR 1596, 1309, 1106, 836 cm^{-1}; HRMS (FAB+) calcd for $C_{38}H_{36}F_{16}N_6O_4$ $[M+H]^+$; 945.2621; found: 945.2615.

4-(2,2,3,3,3-Pentafluoropropoxy)-2-methylpyridine N-oxide (4c) [3d]

Synthesis of **4c** was performed in a similar manner to that of **4b** with 10 mmol of 4-nitro-2-picoline *N*-oxide (1.54 g) and 12 mmol of 2,2,3,3,3-pentafluoro-1-propanol (1.2 mL) at 70 ˚C for 2 h (89% yield) as a yellow solid and subjected to the following reaction without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 7.2 Hz, 1H), 6.83 (d, J = 2.3 Hz, 1H), 6.73 (dd, J = 5.8, 2.1 Hz 1H), 4.41 (t, J = 11.9 Hz, 2H), 2.45 (s, 3H).

(4-(2,2,3,3,3-Pentafluoropropoxy)pyridine-2-yl)methanol (6c) [3d]

The reaction was carried out in a similar manner to the synthesis of **6b** with 4-(2,2,3,3,3-pentafluoropropoxy)-2- methylpyridine *N*-oxide (257 mg, 1.0 mmol) to afford **6c** (167 mg, 2 steps 65%) as a pale yellow oil and subjected to the following reaction. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 5.8 Hz, 1H), 6.94 (d, J = 2.5 Hz, 1H), 6.73 (dd, J = 5.0, 2.3 Hz 1H), 4.68 (s, 2H), 4.44 (*t*, J = 12.0 Hz, 2H).

4-(2,2,3,3,3-Pentafluoropropoxy)-2-(chloromethyl)pyridine (7c)

The reaction was carried out in a similar manner to the synthesis of **7b** with **6c** (4.30 g, 16.7 mmol to give **7c** (3.15 g, 68%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, J = 5.7 Hz 1H), 7.07 (d, J = 2.4 Hz, 1H), 6.80 (dd, J = 5.7, 2.5, Hz, 1H), 4.64 (s, 2H), 4.48 (t, J = 11.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.0, 158.7, 122.0-108.7 (m), 64.1, 64.4, 64.3, 64.1, 63.9; IR 1597, 1314, 1201, 1153, 1105, 1027 cm^{-1}; HRMS (EI+) calcd for $C_9H_7ClF_5NO$ 275.0136; found: 275.0137.

***N,N,N',N'*-tetrakis((4-(2,2,3,3,3-pentafluoropropoxy) pyridine-2-yl) -ethyl)ethane-1,2-diamine (9c)**

The reaction was carried out in a similar manner to the synthesis of **9a** with **6c** (275 mg, 1.0 mmol) with stirring for 5 h at 60 ºC to afford **9c** (89 mg, 35%) as a colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, J = 5.7 Hz 4H), 7.10 (d, J = 2.4 Hz, 4H), 6.70 (dd, J = 5.7, 2.6, Hz, 4H), 4.42 (t, J = 12.1 Hz, 8H), 3.76 (s, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.0, 162.1, 150.7, 120.0-108.9 (m), 64.3, 64.1, 63.8, 60.5, 52.2; IR 1595, 1203, 1152, 1106, 1027, 832 cm^{-1}; mp 75.1-77.2 ˚C; HRMS (FAB+) calcd for $C_{38}H_{32}F_{20}N_6O_4$ $[M+H]^+$:

1017.2244; found: 1017.2244.

4-(2,2,3,3,4,4,4-Heptafluorobutoxy)-2-methylpyridine N-oxide (4d)

Synthesis of **4d** was performed in a similar manner to that of **4b** with 10 mmol of 4-nitro-2-picoline *N*-oxide (1.54 g) and 2,2,3,3,4,4,4-heptafluorobutan-1-ol (1.5 mL, 12 mmol) at 70 ˚C for 2 h (91% yield) as a yellow solid and subjected to the following reaction without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 7.2 Hz, 1H), 6.82 (d, J = 2.8 Hz, 1H), 6.73 (dd, J = 7.2, 3.8 Hz 1H), 4.44 (t, J = 12.3 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 150.4, 140.3, 112.7, 110.5, 65.4, 65.0, 64.7, 18.2; IR 1359, 1474, 1222, 1182, 1124 cm^{-1}.

(4-(2,2,3,3,4,4,4-Heptafluorobutoxy)pyridine-2-yl)methanol (6d).

The reaction was carried out in a similar manner to the synthesis of **6b** with **4d** (257 mg, 1.0 mmol) to afford **6d** (2.17 g, 2 steps 78%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, J = 5.0 Hz, 1H), 6.84 (d, J = 2.4 Hz, 1H), 6.78 (dd, J = 3.4, 1.9 Hz 1H), 4.74 (s, 2H), 4.51 (*t*, J = 12.3 Hz, 2H), ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 150.4, 140.3, 112.7, 110.5, 65.4, 65.0,

64.7, 18.2; IR 1599, 1227, 1126, cm^{-1}.

4-(2,2,3,3,4,4,4-Heptafluorobutoxy)-2-(chloromethyl)Pyridine (7d)

The reaction was carried out in a similar manner to the synthesis of **7b** with **6d** (1.73 g, 5.6 mmol) to give **7d** (0.97 g, 53%) as a colorless solid. ^1H NMR (500 MHz, $CDCl_3$) δ 8.44 (d, J = 5.6 Hz 1H), 7.06 (d, J = 2.5 Hz, 1H), 6.80 (dd, J = 5.7, 2.5 Hz, 1H), 4.63 (s, 2H), 4.50 (t, J = 12.6 Hz, 2H), ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 159.0, 151.1, 109.4, 109.2, 64.6, 64.2, 663.9, 46.4; IR 1597, 1314, 1226, 1125, 1022 cm^{-1}; HRMS (EI+) calcd for $C_{10}H_7ClF_7NO$ 325.0104; found: 325.0107.

***N,N,N',N'*-Tetrakis(4-(2,2,3,3,4,4,4-heptafluorobutoxy)-2-pyridyl methyl)ethylenediamine (9d)**

The reaction was carried out in a similar manner to the synthesis of **9a** with **7d** (127 mg, 0.39 mmol) with stirring for 3.5 h at 60 °C to afford **9d** (88 mg, 74%) as a colorless solid. ^1H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, J = 6.0 Hz, 4H), 7.16 (d, J = 2.5 Hz, 4H), 6.71 (dd, J = 5.7, 2.5 Hz, 4H), 4.47 (t, J = 12.6 Hz, 8H), 3.82 (s, 8H), 2.88 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1,

162.2, 150.7, 108.9, 64.1, 63.8, 60.5, 52.2, 44.6, 43.0; IR 1595, 1226, 1125 cm^{-1}; HRMS (ESI+) calcd for $C_{42}H_{32}F_{28}N_6O_4$ $[M+H]^+$: 1217.2116; found: 1217.2116.

4-(2,2,3,3,4,4,5,5-octafluoropentyloxy)-2-methylpyridine *N*-oxide (4e)

Synthesis of **4e** was performed in a similar manner to that of **4b** with 20 mmol of 4-nitro-2-picoline *N*-oxide (3.08 g) and 2,2,3,3,4,4,5,5-octafluoropentane-1-ol (3.3 mL, 24 mmol) at 70 ˚C for 16 h (66% yield) as a yellow solid and subjected to the following reaction without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 7.2 Hz, 1H), 6.85 (d, J = 3.4 Hz, 1H), 6.75 (dd, J = 7.2, 3.4 Hz 1H), 4.47 (t, J = 12.6 Hz, 2H), 2.51 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.7, 150.5, 140.4, 112.7, 110.5, 65.5, 65.2, 64.8, 18.3; IR 3327, 1416, 1154, 1014, 781 cm^{-1}; HRMS (EI+) calcd for $C_{11}H_9F_8NO_2$ 339.0506; found: 339.0506.

(4-(2,2,3,3,4,4,5,5-octafluoropentyloxy)pyridine-2-yl)Methanol (6e)

The reaction was carried out in a similar manner to the synthesis of **6b** with **4e** (4.35 mg, 12.8 mmol) to afford **6e** as a pale yellow oil and

subjected to the following reaction without further purification. . ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, J = 5.0 Hz, 1H), 6.86 (d, J = 2.2 Hz, 1H), 6.78 (dd, J = 5.7, 2.5 Hz 1H), 6.07 (m, 1H), 4.73 (s, 2H), 4.52 (t, J = 12.9 Hz, 2H). IR 1600, 1169, 1129, 809 cm^{-1}.

4-(2,2,3,3,4,4,5,5-octafluoropentyloxy)-2-(chloromethyl)pyridine (7e)

The reaction was carried out in a similar manner to the synthesis of **7b** with **6e** (4.03 g, 11.9 mmol) to give **7e** (3.47 g, 75%) as a yellow oil.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 5.6 Hz, 1H), 6.96 (d, J = 2.5 Hz, 1H), 6.69 (dd, J = 5.6, 2.5 Hz 1H), 6.02 (m, 1H), 4.51 (s, 2H), 4.44 (t, J = 12.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 158.9, 151.0, 109.3, 109.2, 64.7, 64.3, 46.3; IR 1597, 1107, 1129 cm^{-1}; HRMS (EI+) calcd for $C_{11}H_8ClF_8NO$: 357.0167; found: 357.0168.

***N,N,N',N'*-Tetrakis(4-(2,2,3,3,4,4,5,5-octafluoropentyloxy)-2-pyridyl methyl)ethylenediamine (9e)**

The reaction was carried out in a similar manner to the synthesis of **3a** with **7e** (178 mg, 0.5 mmol) with stirring for 4 h at 60 °C to afford **9e** (132

mg, 78%) as a a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, J = 5.7 Hz, 4H), 7.10 (d, J = 2.5 Hz, 4H), 6.69 (dd, J = 5.6, 2.5 Hz, 4H), 6.06 (m, 1H), 4.46 (*t*, J = 2.1 Hz, 8H), 3.76 (s, 8H), 2.81 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 158.9, 151.0, 118.0-104.3 (m), 64.7, 64.3, 63.9, 46.3; IR 1596, 1170, 1129, 809 cm^{-1}HRMS (FAB+) calcd for $C_{46}H_{36}F_{32}N_6O_4$ $[M+H]^+$: 1345.2365; found: 1345.2367.

4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12-docosafluorododecyl -oxy)-2-methylpyridine *N*-oxide (4f)

Synthesis of **4f** was performed in a similar manner to that of **4b** with 1.0 mmol of 4-nitro-2-picoline *N*-oxide (154 g) and *1H,1H,11H* -eicosafluoro-1-undecanol (638 mg, 1.2 mmol) at 60 ˚C for 15 h (68% yield) as a white solid. ^{1}H NMR (500MHz, $CDCl_3$) δ 8.25 (d, J = 7.2 Hz, 1H), 6.90 (d, J = 3.1 Hz, 1H), 6.81 (dd, J = 7.2, 3.4 Hz 1H), 4.41(t, J = 12.3 Hz, 2H), 2.53 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 154.6, 150.6, 140.4, 112.8-105.6 (m), 65.6, 65.4, 65.2; IR 1595, 1203, 1152, 1106, 1027, 832 cm^{-1}; mp 114.5 – 115.9 ˚C; HRMS (FAB+) calcd for $C_{17}H_9F_{20}NO_2$ $[M+H]^+$: 640.0392; found: 640.0394.

(4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12-docosafluoro -dodecyloxy)pyridine-2-yl) methanol (6f)

The reaction was carried out in a similar manner to the synthesis of **6b** with **4f** (127 mg, 0.2 mmol) to afford **6f** (2.17 g, 2 steps 78%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 5.8 Hz, 1H), 6.94 (d, J = 2.5 Hz, 1H), 6.73 (dd, J = 5.0, 2.3 Hz 1H), 4.68 (s, 2H), 4.44 (t, J = 12.0 Hz, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ 164.2, 162.2, 150.4, 115.0-106.4 (m), 64.8, 64.6, 64.4, 64.3; IR 1603, 1202, 1148, 1074 cm^{-1}; mp 75.5-77.3 ˚C; HRMS (ESI+) calcd for $C_{17}H_9F_{20}NO_2$ $[M+H]^+$: 640.03922; found: 640.03922.

4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12-docosafluoro -dodecyloxy)-2-(chloromethyl) pyridine (7f)

The reaction was carried out in a similar manner to the synthesis of **7b** with **6f** （1.19 g, 1.86 mmol） to give **7f** (1.03 g, 83%) as a colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, J = 5.7 Hz 1H), 7.07 (d, J = 2.4 Hz, 1H), 6.80 (dd, J = 5.7, 2.5, Hz, 1H), 4.64 (s, 2H), 4.48 (t, J = 11.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 159.1, 151.2, 114.8-105.7 (m), 64.8, 64.6, 64.4, 46.4; IR 1595, 1318, 1201, 1150, 1135, 1074 cm^{-1}; mp 64.5-65.7 ˚C; HRMS

(EI+) calcd for $C_{17}H_8ClF_{20}NO$ 656.9975; found: 656.9979.

_N,N,N',N'_-tetrakis(4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-tricosafluorododecyloxy)pyridin-2-yl)methyl)ethane-1,2-diamine (9f)

The reaction was carried out in a similar manner to the synthesis of **3a** with **7f** (65 mg, 0.1 mmol) with stirring for 38 h at 60 ºC to afford **9f** (46 mg, 73%) as a colorless solid. ^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 8.33 (d, J= 5.7 Hz, 4H), 7.35 (d, J= 2.2 Hz, 4H), 6.88 (m, 1H), 6.93 (dd, J= 5.7, 2.5, Hz, 4H), 4.88 (t, J= 13.2 Hz, 8H), 3.78 (s, 8H), 2.82 (s, 4H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 164.5 1, 163.0, 151.0, 109.2-108.7 (m), 65.0, 64.8, 64.5, 60.8, 52.3; IR 1601, 1508, 1260, 1219, 1150, 1024 cm^{-1}; mp 106.5-107.8 ˚C; HRMS (ESI+) calcd for $C_{70}H_{36}F_{80}N_6O_4$ $[M+H]^+$: 2545.15988; found: 2545.15950.

Solvent extraction of Cd^{2+} with fluorinated TPEN derivatives.

A 1 mM of aqueous $Cd(NO_3)_2$ solution was prepared. The pH value of the solution was controlled to 1.1 and 3.5 by the addition of 1 M of aq. NH_4NO_3 and 1 M of HNO_3. TPEN derivative (0.01 mmol) was dissolved in a

10 mL of a solvent. The aqueous $Cd(NO_3)_2$ solution (1 mM) and the organic solutions was stirred vigorously at 25 ºC for 5 min. Aliquot of the aqueous phase (0.8 mL) was taken and diluted with 3.2 mL of distilled water. The resulting solution was subjected to ICP-AES analysis to estimate the concentration of Cd^{2+}. Calculation of %extraction value was performed by the following eqation.

$\%E = 100 \cdot D/(D+1)$, $\{D = ([Cd^{2+}]_{ini}-[Cd^{2+}])/[Cd^{2+}]\}$

$[Cd^{2+}]_{ini}$: concentration of Cd^{2+} in water before extraction;

$[Cd^{2+}]$: concentration of Cd^{2+} in water after extraction.

Table 1 and 2 summarize the results of extraction with chloroform and a fluorous solvent system (HFE7100:$HCH_2CH_2CH_2OH$=10:1), respectively.

Table 1. Extraction of Cd^{2+} by TPEN derivatives with chloroform.

pH[a]		$[Cd^{2+}]_{ini}$ (ppm)	$[Cd^{2+}]$ (ppm)	D	$\%E$	pH_{eq}[b]
3.0	TPEN	22.3	19.4	0.1	12.9	3.2
	F3	23.8	0	-	100	3.2
	F4	23.8	0,0	7475.6	99.9	3.2
	F5	22.2	2.5	7.8	88.7	3.3
	F7	22.3	1.2	17.4	94.5	3.2
	F8	23.8	2.8	17.4	88.1	3.2
	F20	23.8	4.5	4.2	81.0	3.2
2.5	TPEN	22.3	20.1	0.1	9.6	2.6
	F3	24.5	0.0	2986.8	99.9	2.5

	F4	24.5	0.0	1401.2	99.9	2.5
	F5	22.7	2.5	8.0	89.0	2.6
	F7	22.3	1.6	12.3	92.5	2.7
	F8	24.5	5.1	3.7	78.8	2.5
	F20	24.5	11.4	1.1	53.3	2.6
2.0	TPEN	22.5	20.5	0.0	8.5	2.0
	F3	24.5	0.8	28.5	96.6	2.0
	F4	24.5	0.0	445.9	99.7	2.1
	F5	22.8	2.7	7.4	88.1	2.0
	F7	22.5	9.0	1.4	59.9	2.0
	F8	24.5	10.5	1.3	56.9	2.0
	F20	24.5	15.2	0.6	37.9	2.0
1.5	TPEN	22.2	20.1	0.1	9.4	1.6
	F3	24.8	8.1	2.0	67.3	1.6
	F4	24.8	1.1	20.5	95.3	1.6
	F5	22.4	1.6	12.6	92.6	1.6
	F7	22.2	14.0	0.57	36.6	1.6
	F8	24.8	17.9	0.38	27.8	1.5
	F20	24.8	20.0	0.24	19.4	1.6
1.0	TPEN	21.9	20.7	0.0	5.6	1.2
	F3	22.7	18.7	0.2	17.3	1.1
	F4	22.7	11.9	0.9	47.4	1.1
	F5	22.1	3.4	5.4	84.4	1.2
	F7	21.9	19.2	0.1	12.2	1.2
	F8	22.7	20.3	0.1	10.4	1.0
	F20	22.7	22.4	0.0	1.1	1.1

[a] The pH value of initial Cd^{2+} solution. [b] The pH value after equilibrium.

Table 2. Extraction of Cd^{2+} by TPEN derivatives with a fluorous solvent system.

pH[a]		$[Cd^{2+}]_{ini}$ (ppm)	$[Cd^{2+}]$ (ppm)	D	%E	$pH_{eq.}$
3.0	F3	23.9	1.6	13.2	92.9	3.5
	F4	22.5	2.7	5.8	85.4	3.6
	F5	22.5	0.7	28.1	96.5	3.2

	F7	22.5	0.1	204.6	99.5	4.4
	F8	22.2	0.2	109.2	99.0	3.1
	F20	23.9	3.4	5.8	85.4	3.6
2.5	F3	24.5	1.7	13.1	92.9	2.7
	F4	22.6	2.7	7.1	87.6	2.6
	F5	22.6	1.3	15.7	94.0	2.6
	F7	22.6	0.5	38.7	97.4	2.7
	F8	21.6	0.5	36.5	97.3	2.6
	F20	24.5	19.9	4.3	81.2	2.8
2.0	F3	24.4	1.6	13.6	93.1	2.2
	F4	22.5	2.7	7.1	87.6	2.1
	F5	22.5	1.3	15.4	93.9	2.1
	F7	22.5	1.0	20.4	95.3	2.1
	F8	21.2	0.6	32.0	96.9	2.1
	F20	24.4	10.4	1.3	57.2	2.3
1.5	F3	24.3	4.4	4.4	81.5	1.7
	F4	22.3	2.9	6.6	86.8	1.5
	F5	22.3	0.8	26.2	96.3	1.6
	F7	22.3	6.8	2.2	69.4	1.6
	F8	21.3	1.7	11.1	91.7	1.6
	F20	24.3	16.7	0.4	31.2	1.7
1.0	F3	24.7	17.7	0.3	28.3	1.3
	F4	21.9	8.1	1.7	62.9	1.1
	F5	21.9	1.7	11.5	92.0	1.1
	F7	21.9	11.8	0.8	46.2	1.2
	F8	19.7	2.1	8.1	89.1	1.2
	F20	24.7	18.2	0.3	26.3	1.3

[a] The pH value of initial Cd^{2+} solution. [b] The pH value after equilibrium.

NMR experiments.

A $CDCl_3$ solution of 20 mM F5 TPEN (**9c**) was prepared. To the resulting solution was added 10 mM, 20 mM, or 100 mM $CDCl_3$ solution and the mixture was shaken vigorously for 5 min and subjected to the measurement of ^1H NMR spectrum.

V-5 References

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6. HFE7100 (methyl perfluorobutyl ether) was purchased from Sumitomo 3M Ltd.

Chapter VI

Conclusion

In this thesis, the Author focused on the design and synthesis of new chelating agent that could be separate of MA from Ln.

Chapter I

In this chapter, the objective and background of the research were shown. Previous studies and the purpose of this study were also described.

Chapter II

In this chapter, syntheses of TPEN derivatives bearing the different number of the terminal double bond, formation of polymer gels, and extraction studies of a cadmium(II) ion with the synthesized polymer TPEN gel. Synthesized TPEN derivatives with the different number of terminal double bond were synthesized and subjected to copolymerization with NIPA. The polymer gels composed of *N,N,N',N'*-4PPEN and *N,N,N'*-3PPEN were found to be obtained and showed thermo responsive swelling and shrinking behaviors. The TPEN-NIPA gel composed of *N,N,N'*-3PPEN exhibited superior extraction performance at low temperature although the thermo-responsive change of extraction was inferior to *N,N,N',N'*-4PPEN,

while *N,N,N',N'*-4PPEN-NIPA gel showed the excellent temperature-dependent change with slightly lower extraction.

Chapter III

We have synthesized TPEN derivatives bearing different side-chains involving the chain length and the branched structures and the prepared derivatives were subjected to the formation of poly(TPEN-NIPA) gels. The temperature-dependent change of extraction behaviors of cadmium(II) ion with poly(TPEN-NIPA) gels were highly influenced to the side-chain structures. The excellent thermo-responsive change particularly under highly acidic conditions such as pH=ca. 2 would be potentially practical for the chromatographic separation of metal ions, namely thermal swing chromatography, which would be applied for the separation of minor actinides from high level radioactive wastes (HLW). The high performance of TPEN-NIPA gel which synthesized from TPEN derivative bearing methalyloxy substituent is remarkably noteworthy.

Chapter IV

In this chapter, the Author carried out the synthesis of several TEPN derivatives bearing the different number of spacer atoms from ethylenediamine are designed and synthesized. Extraction performance of these derivatives and the corresponding polymer gels that are obtained by the radical copolymerization of TPEN derivatives and NIPA was studied to reveal that the spacer structure was irrespective of the extraction of the cadmium ion in polymer gels as well as liquid-liquid system. Synthesized Polymer gels of showed temperature-dependent swelling and shrinking and thus induced change of the extraction performance, which was also irrespective of the spacer structures. These results suggest that the performance is not significantly influenced by the difference of the spacer structure, while all of these extractants forms 1:1 chelation with cadmium.

Chapter V

In this chapter, the author design and synthesis of several TPEN derivatives bearing fluoroalkyl substituents. The extraction performance of TPEN derivatives was studied with chloroform and a flourous solvent system.

The synthesized TEPN derivatives indicated excellent extraction performance particularly when the extraction was performed with highly acidic aqueous solutions of the cadmium ion.

In conclusion, the author synthesized several TPEN derivatives and the influence of the change of TPEN structure toward the formation of the polymer gel using the TPEN as a cross linker.

Syntheses of TPEN derivatives with different number of the polymerizable double bond, different spacer and branch structure, and different structure of ethylenediamine moiety were carried out. The relation ship of TPEN structure and the extraction behavior of thus obtained TPEN gel was studied.

The author also synthesized several TPEN derivatives bearing fluoroalkyl substituents and employed these TPENs for the solvent extraction of a soft metal ion, cadmium and a minor actinide, americium.

Several TPEN derivatives exhibited excellent extraction performance in such metal ions. These findings suggest that introduction of fluorine atom is an effective way in the design of hydrophobic chelating agents.

List of Publications

Chapter II

1) Thermo-Responsive Extraction of Cadmium(II) Ion with TPEN-NIPA Gel. Effect of The Number of Polymerizable Double Bond Towards Gel Formation and The Extracting Behavior.
Fukuoka, S.; Kida, T.; Nakajima, Y.; Tsumagari, T.; Watanabe, W.; Inaba, Y.; Mori, A.; Matsumura, T.; Nakano, Y.; Takeshita, K. *Tetrahedron*. **2010**, *66*. 1721-1727.

Chapter III

2) Thermo-Responsive Extraction of Cadmium(II) Ion with poly(TPEN-NIPA)gel. Effect of the Chain Length and Branch in the Spacer Structure Towards Gel Formation and the Extracting Behavior
Inaba, Y.; Tsumageri, T.; Kida, T.; Watanabe, W.; Nakajima, Y.; Fukuoka, S.; Mori, A.; Matusmura, T.; Nakano, Y.; Takashita, K. *manuscript in preparation.*

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Chapter IV

3) Temperature-Dependent Change of Extraction Performance of Soft Cadmium(II) Ion with TPEN- NIPA Gel. Studies on the Effect of the Ethylenediamine Skeleton.
Maekawa, T.; Kida, T.; Miyazaki, Y.; Watanabe, W.; Inaba, Y.; Takeshita, K.; Mori, A. *Bull. Chem. Soc. Jpn*. **2011**, *84*, 122-124.

Chapter V

4) Extraction of Cd^{2+} and Am^{3+} Ions into Organic and Fluorous Solvent with a TPEN Chelating Agengt bearing a Fluoroalkyl Substituetnt
Kida, T.; Inaba, Y.; Watanabe, W.; Nakajima, Y.; Fukuoka, S.; Takeshita, K.; Mori. A. *Chem. Lett*. **2010**, *39*, 774-776.

5) Synthesis of TPEN Derivatives bearing a Fluoroalkyl Substituent and Its Extraction Behavior of Soft Metal Ion.
Kida, T.; Miyazaki, Y.; Watanabe, W.; Nakajima, Y.; Inaba, Y.; Takeshita, K.; Mori, A. *manuscript in preparation.*

The Author also contributed to the following paper

6) Synthesis of Highly Oxygenated Biphenyl Derivative in an Optically Active Form through Palladium-Mediated Intramolecular Biaryl Coupling Reaction.
Abe, H.; Arai, M.; Nishioka, K.; Kida, T.; Shioe, K.; Takeuchi, Y and Harayama. T. *Heterocycles*. **2008**, *76*, 291-303.

List of Presentations

1) フルオロアルキル基を有する機能性配位子TPEN誘導体の合成とソフト金属抽出機能評価
Kida, T.; Wataru, W.; Yusuke I.; Mori, A.; Takeshita, K.
The 89th Annual Meeting of The Chemical Society of Japan, Chiba, 2009

2) TPEN誘導体架橋NIPAゲルの合成と機能
Kida, T.; Sachio, F.; Yusuke I.; Mori, A.; Nakano, Y.; Takeshita, K.
高分子研究発表会, Kobe, 2009

3) フルオロアルキル基を有するTPEN誘導体を用いた金属抽出
Kida, T.; Wataru, W.; Yusuke I.; Mori, A.; Takeshita, K.
Symposium on solvent extraction, Osaka, 2009

4) 疎水性置換基を有するTPEN誘導体の合成と機能
喜田達也
若手フロンティア研究会, Kobe, 2009

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