

Extraction of Cd²⁺ and Am³⁺ Ions into Organic and Fluorous Solvents with a TPEN Chelating Agent bearing a Fluoroalkyl Substituent

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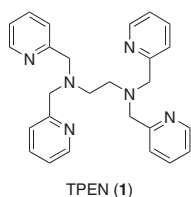
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Introduction of polyfluorinated alkyl groups into TPEN (*N,N,N',N'*-tetrakis(2-pyridylmethyl)ethylenediamine) derivatives provides soft metal ion extracting agents with high acid tolerance. The TPEN derivative bearing a pentafluoropropoxy substituent efficiently extracts Cd²⁺ and Am³⁺ into organic and fluorous solvents.

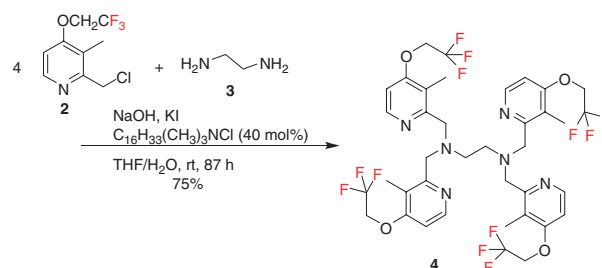
Extraction of metal ions with a chelating agent has recently attracted considerable attention. Much effort has been devoted to the development of effective multidentate chelating agents of metal ions¹ and thereby precise design of organic molecules that bind to a specific ion highly efficiently is intriguing in organic synthesis. In particular, extraction of metal ions such as d-block, lanthanide, and actinide metals is a major concern in the environment, resources, and nuclear electric power generation.^{1a,1b} TPEN (**1**), *N,N,N',N'*-tetrakis(2-pyridylmethyl)ethylenediamine (Chart 1), which possesses six nitrogen donors to capture several metal ions such as cadmium, iron, copper, lanthanides, and actinides, has been a potential chelating agent.² However, a major drawback of TPEN has been water solubility and easy protonation and therefore the use of TPEN as an extracting agent of metal ions particularly in an acidic aqueous solution has been considered to be unlikely. We envisaged 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 cadmium(II) ion from an acidic aqueous solution.^{2a,2b} However, the acid 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 necessary.

On the other hand, fluorocarbons attract much interest in a wide range of fields in organic chemistry, biochemistry, and materials science.³ 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 interac-



TPEN (**1**)

Chart 1.



Scheme 1.

tion 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. Herein, we report syntheses and properties of TPEN derivatives bearing fluoroalkyl substituents on the pyridine rings.

Synthesis of TPEN derivatives bearing a fluoroalkyl substituent on the pyridine ring was first carried out with the reaction of the corresponding 2-(chloromethyl)pyridine **2** and 1,2-ethylenediamine (**3**) as shown in Scheme 1. When 2-chloromethyl-3-methyl-4-(2,2,2-trifluoroethoxy)pyridine (**2**) that was commercially available as a hydrochloride was employed, TPEN derivative **4** was obtained in an excellent yield.⁴ The obtained TPEN derivative was found to be dissolved freely in several organic solvents, while hardly soluble in water.

With the obtained TPEN derivative bearing fluoroalkyl groups **4**, extraction of cadmium(II) ion that serves as a typical soft metal ion was examined.^{2a} A nitric acid solution of Cd(NO₃)₂ (1 mM) was subjected to the extraction with a chloroform solution of **4** (1 mM). The experiments were carried out under various pH values of Cd²⁺ solutions. The percent extraction of Cd was estimated with ICP-AES⁵ by the concentration of the Cd²⁺ ion remaining in an aqueous phase after extraction.

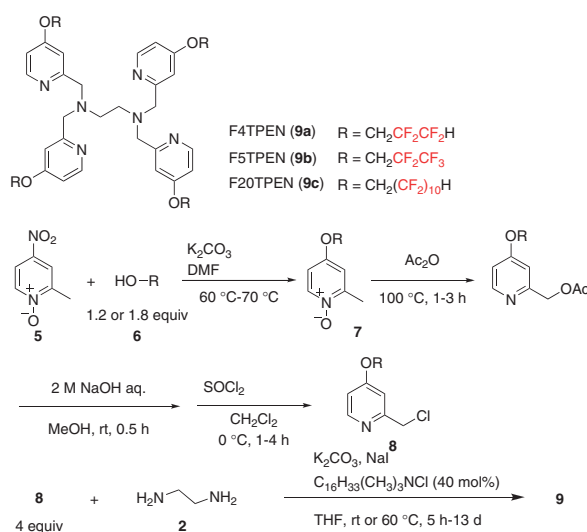
Table 1 shows results of the extraction with TPEN **1**, and the fluorinated derivative **4**. In contrast to the TPEN showing little extraction of Cd²⁺ in the pH range of 1–3, fluorinated TPEN derivative **4** showed remarkable performance in the pH range of ca. 2–3. However, the percent extraction decreased when the aqueous solution became highly acidic (pH < 2). The result suggests that such high extraction performance is achieved by the introduction of fluoroalkyl group showing remarkably high hydrophobic characteristics that inhibit protonation of the nitrogen atoms by the contact with acid in the aqueous phase.

Encouraged by the above results, we envisaged further molecular design of hydrophobic TPEN by the introduction of a longer fluoroalkyl chain. The TPEN derivatives were synthe-

Table 1. Extraction of Cd²⁺ with **1** and TPEN derivative **4**^a

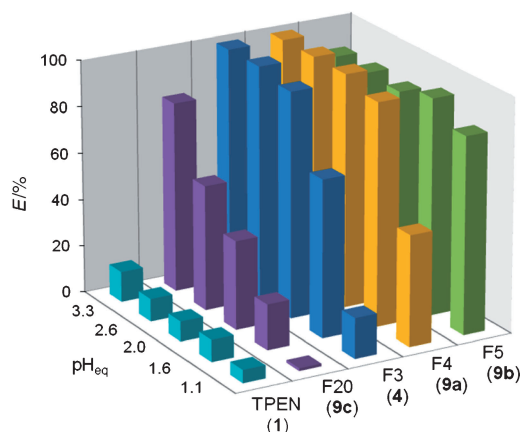
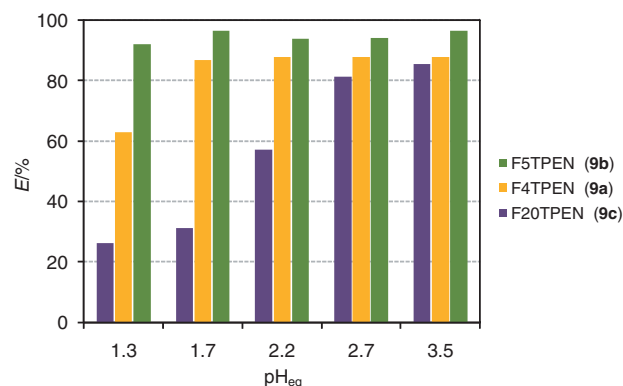
pH	TPEN	eq	pH ^b	%E ^c	TPEN	eq	pH ^b	%E ^c
3.1	1		3.5	12	4		3.3	100
2.7			2.6	9			2.6	100
2.1			2.0	8			2.0	97
1.7			1.6	9			1.7	67
1.2			1.2	5			1.2	17

^aExtraction was performed with 1 mM TPEN derivative in chloroform (1.5 mL) and 1 mM Cd(NO₃)₂ aqueous solution (1.5 mL). ^bThe pH value after equilibrium. ^cThe extracted amount of Cd ion was estimated by ICP-AES analyses of the aqueous solution.

**Scheme 2.**

sized as summarized in Scheme 2 starting from 2-methyl-4-nitropyridine 1-oxide (**5**) and polyfluorinated primary alcohols **6a–6c** in 5 steps. The reaction of **5** with 2,2,3,3-tetrafluoro-1-propanol (**6a**) in the presence of K₂CO₃ at 70 °C for 1 h afforded the corresponding pyridyl ether **7a** in 95% yield. Other fluorinated chloromethylpyridine derivatives also proceeded efficiently to give **7b** and **7c**. The reaction of acetic anhydride, hydrolysis, and chlorination proceeded to afford chloromethylpyridine **8**. The reaction of 1,2-ethylenediamine (**2**) with 4 equivalents of **8** afforded fluorinated TPEN **9** in 35–73% yields.

With the TPEN derivatives **9** bearing a variety of fluoroalkyl substituent in hand, **9** was applied to the extraction of Cd²⁺. Figure 1 summarizes the results of the extraction at various pH with chloroform. The extraction experiment was carried out with a 1 mM chloroform solution of **9** and a 1 mM nitric acid solution of Cd(NO₃)₂. TPEN derivatives bearing tetrafluoropropoxy (F4TPEN, **9a**) and pentafluoropropoxy (F5TPEN, **9b**) substituents showed higher extraction performance at ca. pH 1 than **4**. Such high performance has not been achieved in other extractants as well as TPEN derivatives due to the excellent hydrophobicity of the fluoroalkyl group. On the other hand, a TPEN derivative with longer fluoroalkyl chain length (F20TPEN, **9c**) was found to show inferior extraction to **9a** and **9b**. Indeed, the extraction performance of **9c** was found to decrease at pH < 1.

**Figure 1.** Extraction of Cd²⁺ ion by TPEN derivatives with chloroform.**Figure 2.** Extraction of Cd²⁺ ion by TPEN derivatives bearing fluoroalkyl substituents with fluororous solvent (HFE-7100/H(CF₂)₂CH₂OH).

It should also be pointed out that extraction of Cd²⁺ ions from acidic solution is performed with a fluororous solvent when fluorinated TPEN derivatives **9a** and **9b** are employed. Figure 2 shows the extraction of Cd(NO₃)₂ solution of pH ca. 1–3 with a solution of **9a**, **9b**, and **9c** in a mixture of 10:1 HFE-7100/H(CF₂)₂CH₂OH.^{6,7} It was found that **9a** and **9b**, which contain four or five fluorine atoms in a side chain, showed high extraction performance. The results clearly indicate that the fluororous solvent system is highly effective for **9** to extract Cd²⁺ ion.

Several actinides are also a class of candidate metal ions and extraction of actinides has been a major concern in atomic power generation.^{1a,1b} Separation of minor actinides (MA) such as Am³⁺ and Cm³⁺, which are obtained during the reprocessing of spent nuclear fuel, as a mixture of lanthanides(III), is an indispensable process for the treatment of high level radioactive waste (HLW). Thus, reduction of the term of the underground repository of HLW to ca. 300 years from 10⁴ years can be achieved if the long-half-lived radioactive Am³⁺ and Cm³⁺ is removed from HLW.¹ Despite tremendous efforts toward the development of a selective and effective extracting agent for MAs from lanthanides there still lacks the practical solution so far. Although TPEN has also been shown to be a possible candidate as a separating agent that can recognize small

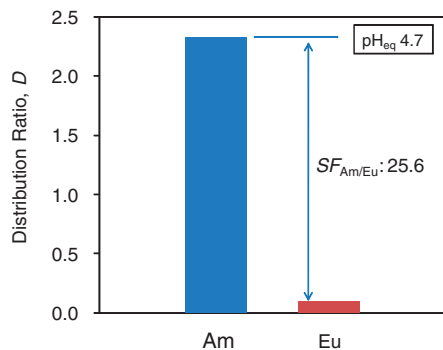


Figure 3. Extraction of $^{241}\text{Am}^{3+}$ and $^{152}\text{Eu}^{3+}$ with 1 mL of 1 mM fluoruous solvent (HFE-7100/ $\text{H}(\text{CF}_2)_2\text{CH}_2\text{OH}$) of **9b** from 1 mL of 0.01 M NaNO_3 aqueous solution containing 610:1 mixture of ^{152}Eu (103 Bq mL^{-1}) and ^{241}Am (495 Bq mL^{-1}).

differences in the softness of MAs and lanthanides, insufficient acid tolerance as well as a high water solubility has been problems for the practical application.^{1a,2j-2m}

A TPEN derivative F5 (**9b**) was thereby applied to the separation of Am^{3+} and Eu^{3+} with a fluoruous solvent. Extraction of an aqueous solution of radioactive ^{241}Am and ^{152}Eu was performed with 10:1 of HFE-7100/ $\text{H}(\text{CF}_2)_2\text{CH}_2\text{OH}$. Preliminary studies revealed selective extraction when the extraction was carried out with a 610:1 mixture of ^{152}Eu (103 Bq mL^{-1}) and ^{241}Am (495 Bq mL^{-1}) in 0.01 M of NaNO_3 aqueous solution (1 mL) at pH of 4.0 and 1 mM HFE-7100/ $\text{H}(\text{CF}_2)_2\text{CH}_2\text{OH}$ (10:1) solution of **9b** (1 mL) providing a distribution ratio of 2.33 (Am) and 9.11×10^{-2} (Eu), respectively, indicating that the separation factor of Am/Eu is 25.6 (Figure 3).⁸ It should be noted that extraction of MAs with a fluoruous solvent is successfully shown for the first time using fluorinated TPEN derivative **9b** with a remarkably high separation factor, although further studies are necessary for practical separation of HLW including experiments with a more acidic Am/Eu solution to achieve selective extraction.

In summary, several TPEN derivatives bearing fluoroalkyl substituents were synthesized and applied to the extraction of the soft metal ion Cd^{2+} and a minor actinide Am^{3+} . TPENs bearing tetrafluoro- or pentafluoropropoxy groups exhibited excellent extraction performance particularly from highly acidic aqueous solutions, which would be potentially effective in the reprocessing of HLW. It was also found that extraction was efficiently performed with a fluoruous solvent system that would be a new class of solvent extraction system. This suggests that introduction of fluoroalkyl group into other existing extracting agents for metal ions improves the extraction performance if appropriate molecular design is done.⁹

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References and Notes

- For reviews, see: a) Z. Kolarik, *Chem. Rev.* **2008**, *108*, 4208. b) V. K. Manchanda, P. N. Pathak, *Sep. Purif. Technol.* **2004**, *35*, 85. c) B. S. Creaven, D. F. Donlon, J. McGinley, *Coord. Chem. Rev.* **2009**, *253*, 893. d) L. D. Nghiem, P. Mornane, I. D. Potter, J. M. Perera, R. W. Cattrall, S. D. Kolev, *J. Membr. Sci.* **2006**, *281*, 7. e) F. Marchetti, C. Pettinari, R. Pettinari, *Coord. Chem. Rev.* **2005**, *249*, 2909.
- a) T. Ogata, K. Takeshita, G. A. Fugate, A. Mori, *Sep. Sci. Technol.* **2008**, *43*, 2630. b) T. Ogata, K. Takeshita, K. Tsuda, A. Mori, *Sep. Purif. Technol.* **2009**, *68*, 288. c) K. Shimojo, H. Naganawa, J. Noro, F. Kubota, M. Goto, *Anal. Sci.* **2007**, *23*, 1427. d) Y. Mikata, A. Yamanaka, A. Yamashita, S. Yano, *Inorg. Chem.* **2008**, *47*, 7295. e) C. A. Blindauer, M. T. Razi, S. Parsons, P. J. Sadler, *Polyhedron* **2006**, *25*, 513. f) K. Takeshita, K. Watanabe, Y. Nakano, M. Watanabe, *Hydro-metallurgy* **2003**, *70*, 63. g) K. Takeshita, K. Watanabe, Y. Nakano, M. Watanabe, *Chem. Lett.* **2003**, *32*, 96. h) I. Cukrowski, E. Cukrowska, R. D. Hancock, G. Anderegg, *Anal. Chim. Acta* **1995**, *312*, 307. i) N. Hirayama, S. Iimuro, K. Kubono, H. Kokusen, T. Honjo, *Talanta* **1996**, *43*, 621. j) M. P. Jensen, L. R. Morss, J. V. Beitz, D. D. Ensor, *J. Alloys Compd.* **2000**, *303–304*, 137. k) M. Watanabe, R. Mirvaliev, S. Tachimori, K. Takeshita, Y. Nakano, K. Morikawa, R. Mori, *Chem. Lett.* **2002**, *1230*. l) R. Mirvaliev, M. Watanabe, T. Matsumura, S. Tachimori, K. Takeshita, *J. Nucl. Sci. Technol.* **2004**, *41*, 1122. m) C. Ekberg, A. Fermvik, T. Retegan, G. Skarnemark, M. R. S. Foreman, M. J. Hudson, S. Englund, M. Nilsson, *Radiochim. Acta* **2008**, *96*, 225. n) T. Matsumura, Y. Inaba, A. Mori, K. Takeshita, *J. Nucl. Sci. Technol.* **2010**, *47*, 123.
- For reviews, see: a) J. A. Gladysz, D. P. Curran, I. T. Horváth, *Handbook of Fluorous Chemistry*, Wiley-VCH, Weinheim, **2004**. b) P. Kirsch, *Modern Fluoroorganic Chemistry*, Wiley-VCH, Weinheim, **2004**. c) W. Zhang, *Chem. Rev.* **2009**, *109*, 749. d) D. P. Curran, *J. Fluorine Chem.* **2008**, *129*, 898.
- Synthesis of TPEN derivatives were carried out by following the literature method with slight modification, see: a) M. Tamura, Y. Urano, K. Kikuchi, T. Higuchi, M. Hirobe, T. Nagano, *Chem. Pharm. Bull.* **2000**, *48*, 1514. b) L. Karmazin, M. Mazzanti, J.-P. Bezombes, C. Gateau, J. Pécaut, *Inorg. Chem.* **2004**, *43*, 5147. c) M. Sato, Y. Mori, T. Iida, *Synthesis* **1992**, 539.
- G. V. Myasoedova, O. B. Mokhodoeva, I. V. Kubrakova, *Anal. Sci.* **2007**, *23*, 1031.
- Recent studies using HFE-7100, see: a) S. R. Livingston, C. C. Landry, *J. Am. Chem. Soc.* **2008**, *130*, 13214. b) C. del Pozo, A. I. Keller, T. Nagashima, D. P. Curran, *Org. Lett.* **2007**, *9*, 4167. c) S. Shimizu, T. Kiuchi, N. Pan, *Angew. Chem., Int. Ed.* **2007**, *46*, 6442. d) D. P. Curran, R. Bajpai, E. Sanger, *Adv. Synth. Catal.* **2006**, *348*, 1621.
- HFE-7100 (methyl perfluorobutyl ether) was purchased from Sumitomo 3M Ltd.
- See Supporting Information.
- Supporting Information is available electronically on the CSJ-Journal Web site, <http://www.csj.jp/journals/chem-lett/index.html>.