

ORIGINAL ARTICLE

Thermoresponsive extraction of cadmium(II) ions by poly(TPEN–NIPA) gels. Effect of chain length and branched spacer structure on gel formation and extraction behavior

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N,N,N',N'-(tetrakis-2-pyridylmethyl)ethylenediamine (TPEN) derivatives bearing a polymerizable double bond in the substituent structure of the pyridine ring were synthesized and subjected to copolymerization with *N*-isopropylacrylamide in the presence of azobisisobutyronitrile. The obtained poly(TPEN–NIPA) gels show thermoresponsive swelling/shrinking behaviors, and are used for the extraction of cadmium(II) (Cd^{II}) ions from an aqueous solution to examine the relationship between gel characteristics and extraction performance. Polymer gels composed of TPEN derivatives bearing C3, C4, C10 and branched C3 spacer chains were synthesized, and the temperature-dependent Cd ion extraction behaviors of the gels were compared. The gels extracted Cd^{II} ions efficiently from the aqueous solution in a swelling state at 5 °C, whereas little extraction was observed at 45 °C in the shrinking state. Poly(TPEN–NIPA) gel with branched C3 spacers (C3b) shows excellent thermoresponsive extraction performance. *Polymer Journal* (2011) 43, 630–634; doi:10.1038/pj.2011.38; published online 27 April 2011

Keywords: Cd^{II} extraction; number of double bonds; poly(TPEN–NIPA) gel; thermoresponsive swelling and shrinking; TPEN

INTRODUCTION

Functionality design based on outside stimuli has attracted considerable attention in a wide range of fields. A polymer gel composed of poly(*N*-isopropyl acrylamide) (poly-NIPA), which reversibly switches between swelling and shrinking corresponding to temperature changes, is therefore intriguing as a thermoresponsive functional material.^{1–4} We have recently shown that poly(*N,N,N',N'*-(tetrakis-2-pyridylmethyl)ethylenediamine (TPEN)–NIPA) gel effectively extracts soft metal ions such as cadmium(II) (Cd^{II}), and its extraction behavior is thermally dependent in various pH regions. The gel was shown to extract Cd^{II} at low temperatures, whereas little extraction was observed at elevated temperatures.^{5–8} *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 and Pd.^{9–13} It was also shown to be effective for the chelation of *f*-block metals; the separation of minor actinides from high-level radioactive waste is a pressing issue.^{14–23} Derivatives of TPEN have been used as extracting agents for a variety of metal ions in organic solvents. However, it is possible to extract metal ions from aqueous solutions without organic solvent if the

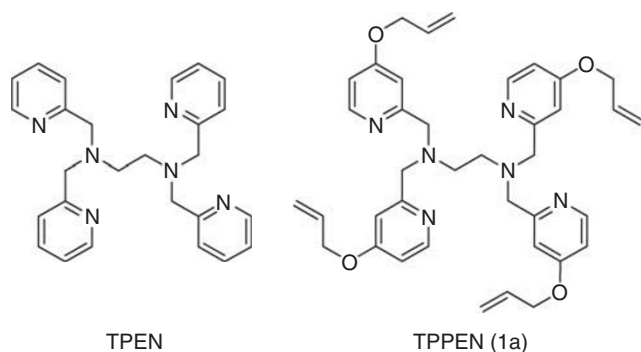
TPEN moiety is incorporated into a polymer gel. Because poly-NIPA gel has been shown to swell at low temperatures in water and shrink at temperatures higher than the lower critical solution temperature,¹ this thermoresponsive swelling/shrinking can function as a conformational change that induces temperature-dependent changes in TPEN extraction behavior when a TPEN moiety such as **1a** is used as a crosslinker in poly-NIPA gel.

In a recent report, we used the temperature-dependent extraction of Cd^{II} ions to study the relationship between the number of polymerizable double bonds in the pyridine ring and the structure of the ethylenediamine moiety on TPEN derivatives.^{7,8,24–29} It was shown that poly(TPEN–NIPA) gel must be prepared from TPEN derivatives bearing at least three double-bond moieties to form a stable polymer gel and to show temperature-dependent changes in extraction behaviors. Accordingly, our concern centers on the relationship between the chain length and the branched structure of the spacer moiety between the polymer main chain and TPEN moiety. In this study, we report the synthesis of several TPEN derivatives bearing four polymerizable double bonds in the substituent on the pyridine ring with different methylene spacer lengths and branched structures. We also

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Received 24 February 2011; revised 15 March 2011; accepted 16 March 2011; published online 27 April 2011



Scheme 1 TPEN derivatives.

study the temperature-dependent Cd ion extraction behaviors of poly(TPEN–NIPA) gels with different spacer structures (Scheme 1).

EXPERIMENTAL PROCEDURE

General

NMR (500 MHz for ^1H , 125 MHz for ^{13}C) spectra were acquired using a Bruker Avance 500 spectrometer (Bruker BioSpin, Yokohama, Japan) at the Center for the Support of Research and Education Activities, Kobe University. Chemical shifts are expressed in p.p.m. using tetramethylsilane as an internal standard (0 p.p.m.). Coupling constants (J) are shown in hertz (Hz). Infrared (attenuated total reflectance) spectra were measured with a Bruker Optics (Tokyo, Japan) Alpha spectrometer with Ge. TLC analyses were performed on analytical TLC plates coated with 60 F₂₅₄ (E Merck, Tokyo, Japan) silica gel or alumina on aluminum foil. Column chromatography was performed using silica gel Wakogel C200 (Wako Chemicals, Kanagawa, Japan) or basic alumina (Wako Chemicals or Merck). High-resolution mass spectra were measured at the Nara Institute of Science and Technology with a JEOL JMS-700 (JEOL, Tokyo, Japan). ICP–AES analysis was carried out with a SII SPS3100 (SII, Chiba, Japan) at the Center for the Support of Research and Education Activities of Kobe University.

Chemicals were used as purchased, without further purification.

Chloromethylpyridine derivatives were prepared in the manner described previously. The spectroscopic characteristics and physical properties are given below.

2-Chloromethyl-4-(buta-3-en-1-yloxy)pyridine (6b)

^1H 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) 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+) calculated for $\text{C}_{10}\text{H}_{12}\text{ClNO}$ [M] $^+$: 197.0607; found: 197.0604.

2-Chloromethyl-4-(deca-9-en-1-yloxy)pyridine (6c)

^1H 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) 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 $\text{C}_{16}\text{H}_{24}\text{ClNO}$ [M] $^+$: 281.1546; found: 281.1541.

2-Chloromethyl-4-(2-methylprop-2-en-1-yloxy)pyridine (6d)

^1H 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) 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 $\text{C}_{10}\text{H}_{12}\text{ClNO}$ [M] $^+$: 197.0607; found: 197.0607.

N,N,N',N' -Tetrakis[4-(buta-3-en-1-yloxy)pyridin-2-ylmethyl]ethylenediamine (1b)

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) were added to a 25-ml round-bottom flask under nitrogen atmosphere. To those compounds, 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. ^1H 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) 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 $\text{C}_{42}\text{H}_{52}\text{N}_6\text{O}_4$ [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 tetrahydrofuran/toluene (1:1, 0.5 ml), **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 were successively added. The reaction mixture was stirred for 19 h at 50 $^\circ\text{C}$. 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. ^1H 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) 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+) calculated for $\text{C}_{66}\text{H}_{100}\text{N}_6\text{O}_4$ [$\text{M}+\text{H}$] $^+$: 1041.7884; found: 1041.7894.

N,N,N',N' -Tetrakis[4-(2-methylprop-2-en-1-yloxy)pyridin-2-ylmethyl]ethylenediamine (1d)

To a solution of ethylenediamine (4.02 μl , 0.06 mmol) in tetrahydrofuran (0.482 ml), **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, 0.12 mmol) under nitrogen atmosphere were successively added. The reaction mixture was stirred for 22 h at 50 $^\circ\text{C}$. 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. ^1H 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) 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 $\text{C}_{42}\text{H}_{52}\text{N}_6\text{O}_4$ [M] $^+$: 704.4050; found: 704.4044.

General procedure for the radical polymerization of NIPA with TPEN derivatives

To a 25-ml sealed tube, equipped with a magnetic stirring bar, *N*-isopropylacrylamide (170 mg, 1.5 mmol) and TPEN derivative (0.019 mmol) were added. The mixture was dissolved in 0.13 ml of DME, and azobisisobutyronitrile (1.25 mol % or 2.50 mol %) was added in one portion. The resulting mixture was heated at 60 $^\circ\text{C}$ for 18 h. The mixture was then cooled to room temperature and repeatedly washed with water. Poly(TPEN–NIPA) gels (**C3**, **C4**, **C10** and **C3b**; see Scheme 3) obtained were found to swell in water at room temperature and shrink when the mixture was heated to 45 $^\circ\text{C}$.

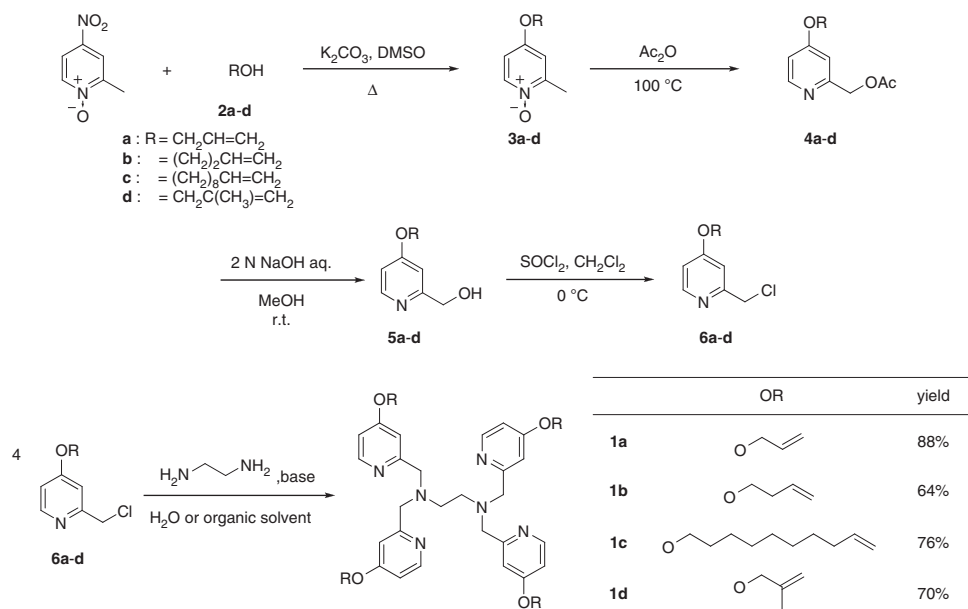
Extraction of cadmium(II) ion by poly(TPEN–NIPA) gel

An aliquot of poly(TPEN–NIPA) gel swollen in water was placed in a flask, and water was removed by heating at 50 $^\circ\text{C}$ under reduced pressure to leave a

Table 1 Extraction of Cd^{II} by TPEN derivatives

poly(TPEN-NIPA) gel	Weight of dry gel (mg)	Temp. (in °C)	pH (Before extraction)	pH (After extraction)	Cd absorbed (mmol per g-dry gel)
C3	7.8	5	1.9	2.3	3.20 × 10 ⁻²
			5.3	6.3	7.91 × 10 ⁻²
			2.0	2.5	1.07 × 10 ⁻²
C4	7.8	5	1.9	2.3	4.64 × 10 ⁻²
			5.3	6.3	9.57 × 10 ⁻²
			2.0	2.4	0.48 × 10 ⁻²
C10	8.4	5	1.9	2.3	5.50 × 10 ⁻²
			5.3	4.3	9.13 × 10 ⁻²
			2.0	2.4	1.64 × 10 ⁻²
C3b	7.8	5	1.9	2.5	6.40 × 10 ⁻²
			5.3	6.5	9.60 × 10 ⁻²
			2.0	2.3	0.26 × 10 ⁻²
			5.9	6.7	0.01 × 10 ⁻²

Abbreviations: Cd, cadmium; NIPA, *N*-isopropylacrylamide; Temp., temperature; TPEN, *N,N,N',N'*-(tetrakis-2-pyridylmethyl)ethylenediamine.

**Scheme 2** Synthesis of TPEN derivatives.

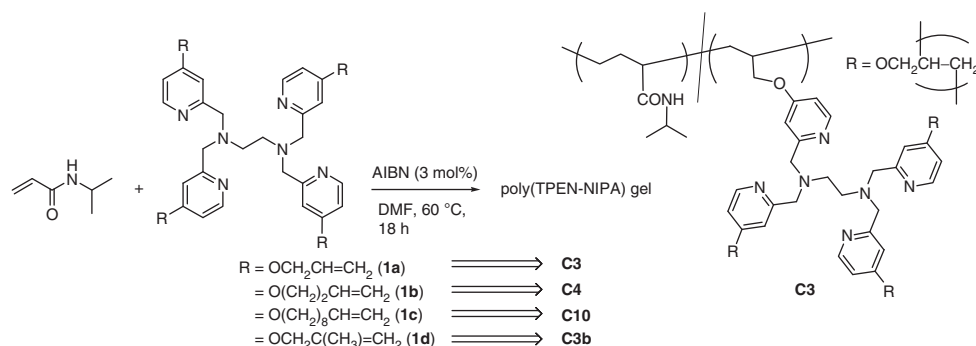
colorless solid, which was used for the extraction. A 1-mM aqueous Cd(NO₃)₂ solution was prepared. The pH values of the solutions were adjusted to 1.9, 2.0, 5.3 and 5.9 by controlled addition of 1-M aqueous NH₄NO₃ and 1-M HNO₃. Poly(TPEN-NIPA) gel (2.5 mol% concentration of TPEN contents at the polymerization reaction) with a controlled TPEN moiety concentration of 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 or 45 °C. An aliquot of the solution (0.2 ml) was taken, passed through a membrane filter (0.2 μm), and diluted with distilled water to 4 ml; it was then subjected to ICP-AES analysis. The amounts of Cd^{II} absorbed by poly(TPEN-NIPA) dry gels (mmol per g dry gel) are summarized in Table 1.

RESULTS AND DISCUSSION

The synthetic pathways of TPEN derivatives with different side-chain lengths (1a-c) and branched structures (1d) are summarized in Scheme 2. Syntheses of pyridine derivatives bearing allyloxy moieties

3a-6a and TPEN derivative 1a were previously reported.⁵⁻⁷ Reactions affording 3b-d, 4b-d, 5b-d and 6b-d were conducted in similar manners. Although the reaction of 2-methyl-4-nitropyridine-1-oxide with allylic alcohol 2a or 2d proceeded smoothly, harsh conditions were necessary to afford 3b and 3c. Other reactions involving the introduction of the OAc group, hydrolysis of the acetoxy group and chlorination proceeded similarly. The obtained chloromethyl pyridine derivatives 6 were subjected to reaction with 1,2-ethylenediamine to afford the corresponding TPEN derivatives with substituents 1b-d. TPEN derivative 1b, which bears a 3-butenyloxy group at the 4-position of the pyridine ring, is a homologated derivative of 1a, whereas 1c (R=9-decen-1-yl) involves longer methylene groups. Derivative 1d possesses a methyl group at the C-2 carbon atom as a branched structure.

The TPEN derivatives, thus obtained, were subjected to radical copolymerization, leading to poly(TPEN-NIPA) gel (Scheme 3).



Scheme 3 Synthesis of poly(TPEN-NIPA) gel.

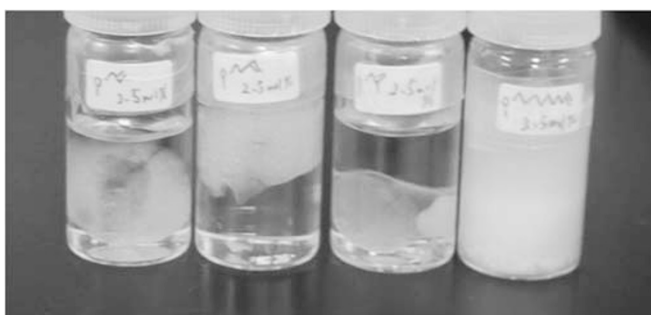


Figure 1 *N,N,N',N'*-(tetrakis-2-pyridylmethyl)ethylenediamine-*N*-isopropylacrylamide (TPEN-NIPA) gels **C3**, **C4**, **C3b** and **C10** (left to right) in water.

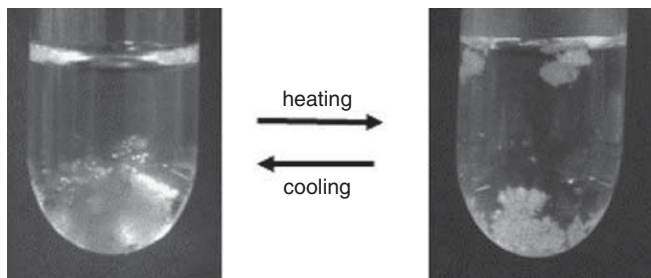


Figure 2 Thermoresponsive swelling and shrinking behaviors of **C4**.

The reaction was performed with NIPA and TPEN derivatives **1a–d** in the presence of azobisisobutyronitrile as a radical initiator in DMF. All of the polymerizations were carried out at 60 °C for 18 h. When 1.25 mol% concentrations of TPEN derivatives **1a**, **1b** and **1d** were used, the obtained polymer gels were insoluble in water (**C3**, **C4** and **C3b**, respectively). In contrast, polymerization with **1c** resulted in insufficient gel formation, and product **C10** mostly dissolved after being placed in water for 2 days. Improved gel formation was observed with 2.50 mol% **1c**, but slow leaching into the water was still found to be inevitable. The obtained polymer gels were found to be insoluble in any organic solvent or water; spectroscopic analyses of the chemical structures of the gels were therefore totally unsuccessful. Figure 1 shows poly(TPEN-NIPA) gels **C3**, **C4**, **C3b** and **C10** in water in a swollen state.

The obtained gels were dried by heating at 50 °C under reduced pressure to afford colorless powders. In aqueous solutions, the gels showed repeated swelling at room temperature and shrinking when heated. The volume changes between swollen and shrinking states were found to be 25 (**C3**) and 18% (**C10**), respectively. Figure 2 shows the representative thermoresponsive change of **C4**.

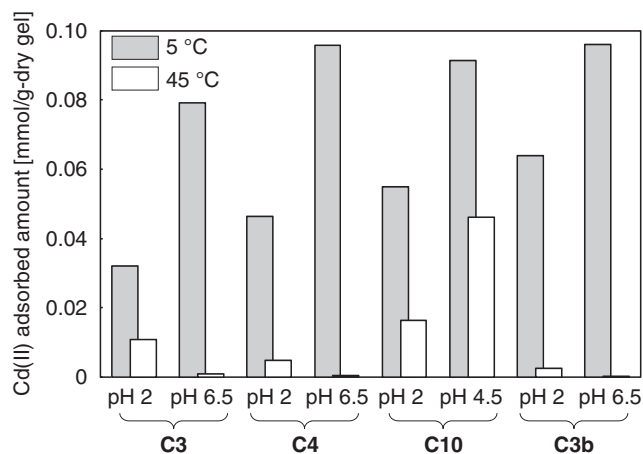


Figure 3 Thermoresponsive extraction by poly(*N,N,N',N'*-(tetrakis-2-pyridylmethyl)ethylenediamine-*N*-isopropylacrylamide (TPEN-NIPA) gels at 5 and 45 °C.

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 because of the improved reactivity brought about by the introduction of an electron-donating methyl substituent into the double bond. In contrast, the performance of poly(TPEN-NIPA) gel **C10** was inferior to other gels, partially dissolving in water on standing. This could be due to the longer, more flexible methylene chains, which inhibit stiff crosslinking.

Extraction studies were carried out on poly(TPEN-NIPA) gels using Cd^{II} ion. Temperature-dependent extraction behavior was examined in the swollen state (5 °C) and in the shrinking state (45 °C) at pH values of ~2.0 and 6.5, respectively. A 1-mM solution of Cd(NO₃)₂ was prepared, and the pH values were adjusted to 1.9 and 5.3 (at 5 °C) for the swollen-state gels and to 2.0 and 5.9 (45 °C) for the shrinking-state gels by the addition of NH₄NO₃. Extraction was performed by the addition of dried poly(TPEN-NIPA) gel to 0.2 ml of 1-mM Cd(NO₃)₂ solution. The amount of Cd^{II} ion incorporated into the gel was estimated by ICP-AES analysis of the remaining amount of Cd ion. Figure 3 summarizes the results.

As reported previously, **C3** extracted Cd ion efficiently at 5 °C (7.91×10^{-2} mmol-Cd per g dry gel) when the extraction was performed at pH 6.5, whereas at 45 °C, it extracted hardly any Cd^{II} (0.08×10^{-2}). Such behavior was also observed at pH \approx 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 Cd^{II} extracted and the thermo-responsive difference (for pH \approx 2, 4.64×10^{-2} at 5 °C, 0.48×10^{-2}

at 45 °C). This improvement in performance could be due to the homologation of the side chain, which would increase the hydrophobicity of the TPEN moiety.¹⁶ C10 also showed improved extraction performance for both pH levels near 2 and 4.5 (5 °C; 5.50×10^{-2} , 9.13×10^{-2}). This could also be due to the increased hydrophobicity of long methylene chains. However, extraction performance in the shrinking state at 45 °C unexpectedly improved, leading to an inferior thermoresponsive change at pH values 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 performance in the swelling state and a thermoresponsive change at pH 6.5, resulting in the highest extraction at 5 °C and low extraction at 45 °C. Also noteworthy was its remarkably high extraction at pH 2 and at 5 °C (6.40×10^{-2}), and its excellent thermoresponsive change (6.40×10^{-2} to 0.26×10^{-2}). This could be due to the formation of a stiff gel as well as the increased hydrophobicity.

CONCLUSION

In summary, we have synthesized TPEN derivatives bearing side chains with varying chain length and branched structures. The prepared derivatives were used to form poly(TPEN-NIPA) gels. The temperature-dependent change in the Cd^{II} ion extraction behavior of poly(TPEN-NIPA) gels was highly influenced by the side-chain structures. The excellent thermoresponsive changes observed, particularly under highly acidic conditions (pH ≈ 2), could potentially be used for the chromatographic separation of metal ions, specifically for thermal swing chromatography, which could be applied toward the separation of minor actinides from high-level radioactive wastes. The high performance of TPEN-NIPA gel C3b is noteworthy.

ACKNOWLEDGEMENTS

This work was partially supported by the Innovative Nuclear Research and Development Program of the Ministry of Education, Sports, Culture, Science, and Technology (MEXT), Japan. We thank the Support Network for Nanotechnology Research of the Nara Institute of Science and Technology supported by MEXT for the measurement of high-resolution mass spectra.

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