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Thermo-responsive extraction of cadmium(II) ion with TPEN-NIPA gel. Effect of the number of polymerizable double bond toward gel formation and the extracting behavior

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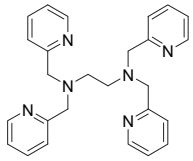
ABSTRACT

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 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 three or four double bonds exhibit temperature-dependent change of swelling and shrinking in water. These gels extract Cd^{II} ion efficiently from the aqueous solution in the swelling state at 5 °C, while little extraction was observed at 45 °C with shrinking.

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.[3b] 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**)

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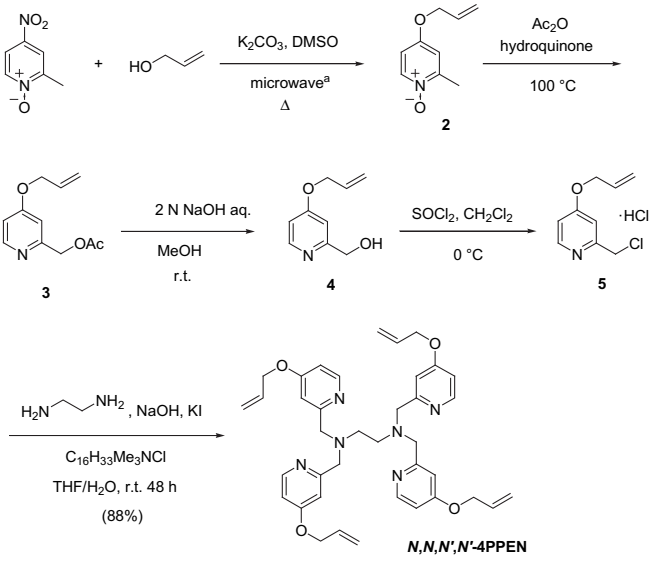
In our previous works, we have shown that a TPEN-NIPA gel was synthesized by radical polymerization of NIPA in the presence of a TPEN derivative bearing four polymerizable double bonds on the pyridine ring and showed temperature-dependent change of extraction behavior of Am^{III} and Cd^{II}, which was recognized as a model metallic species of MAs.[7] The TPEN-NIPA gel effectively extracted Cd^{II} ion at swelling state (5 °C), while little extraction of Cd^{II} ion was confirmed at the elevated temperature (45 °C) where shrinking of the gel was 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 temperature-dependent extraction behaviors of a Cd^{II} ion[8] with the obtained TPEN-NIPA gel.

2. Results and discussion

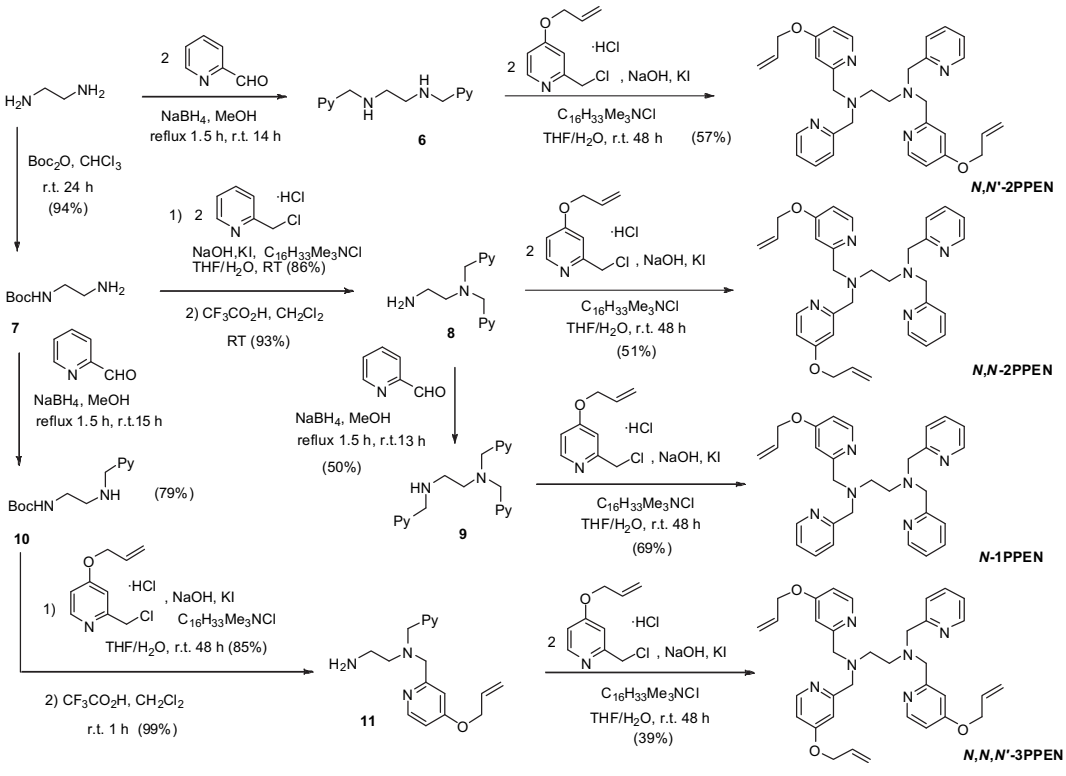
Synthesis of TPEN derivatives bearing the different number of the polymerizable functional group was carried out as outlined in Schemes 1 and 2. The synthetic strategy was based on the controlled introduction of functionalized and unsubstituted chloromethylpyridine derivatives into ethylenediamine. Chloromethylpyridine 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).

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.

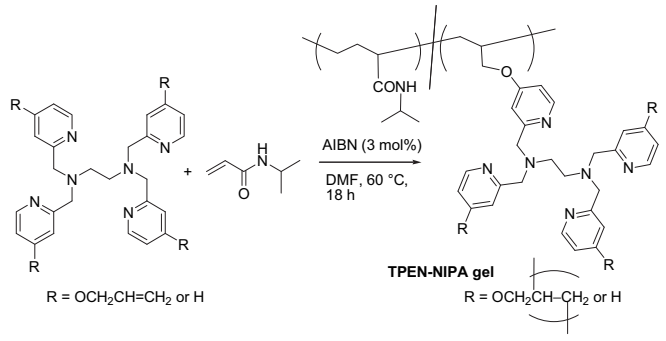
Other TPEN derivatives were synthesized with *N*-Boc-ethylenediamine **7**, which was prepared by the reaction of ethylenediamine with $(Boc)_2O$.[10] The reaction of **7** with chloromethylpyridine hydrochloride in the manner for the reaction of **6** and **5** and following removal of the Boc group 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**



Scheme 1.



Scheme 2.



Scheme 3.

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**.

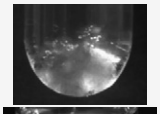
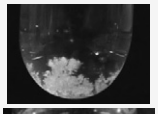
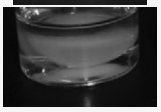
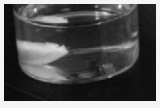
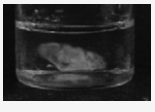
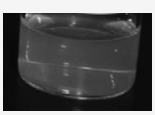
All of the TPEN derivatives bearing the different number of the double bond were synthesized in reasonable yields. Worthy of note is the modified protocol of the reaction of chloromethylpyridine with an amino group. Conventional synthesis of TPEN has been performed by the reaction of chloromethylpyridine **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).

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 °C) and the shrinking state (45 °C) at the pH value of 2.1 and 5.3, respectively. As summarized in Figure 1, the percent extraction value (%*E*) of Cd^{II} 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

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[a]

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) (2.50)	Partially water soluble 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 °C for 18 h.
[b] Prepared in a manner shown in Ref 6.
[c] Swollen (left); shrinked (right).

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 °C highly efficiently, while the extraction performance at 45 °C was much inferior to those at 5 °C. The results suggest that excellent extraction of cadmium(II) ion is observed in the swelling state, while the gel hardly extracted Cd^{II} in the shrinking state at 45 °C. A slightly higher extraction at 45 °C 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^{II} at 5 °C, while no extraction was observed at the shrinking state (45 °C). 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.

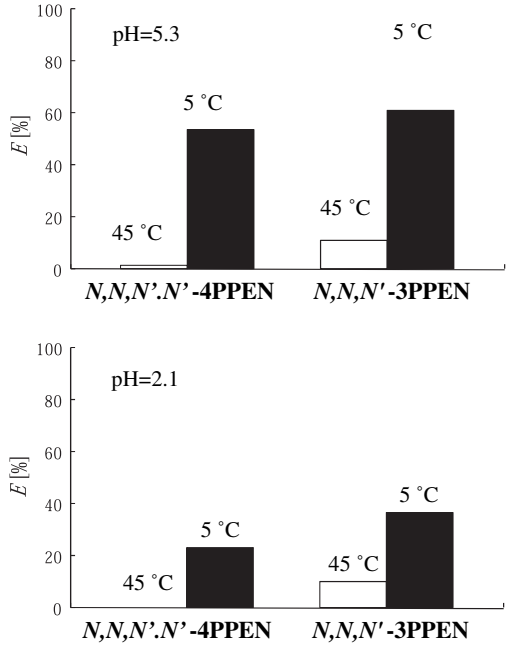


Figure 1. Temperature-dependent extraction of Cd^{II} ion with *N,N,N′,N′*-4PPEN-NIPA gel and *N,N,N′*-3PPEN-NIPA gel at pH 5.3 (top) and pH 2.1 (down).

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 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.

4. Experimental section

4.1. General

NMR (500 MHz for ^1H, 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 Activities 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.

*4.1.1. 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.

*4.1.2. 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 satd 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 °C, large amount of diethyl ether was added and the solvent was evaporated to afford hydrochloride salt. ^1H 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:$C_9H_{10}ClNO$).

*4.1.3. 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.

*4.1.4. 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 satd 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.

*4.1.5. (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).

*4.1.6. 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).

*4.1.7. 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.

*4.1.8. 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).

*4.1.9. 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 H_2O (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 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*-1PPEN (99.8 mg, 0.21 mmol) in 69% yield. ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 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.

*4.1.10. {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 satd 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).

*4.1.11. 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) ethylenediamine (**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.

4.2. 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** and **3PPEN**, which was estimated by the observation of the volume change of both states.

4.3. 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 5 °C 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, which was subjected to ICP-AES analysis. The percent extraction value was calculated as.

$$\%E = 100 \cdot D/(D+1), \quad \left\{ D = \left(\left[Cd^{II} \right]_{ini} - \left[Cd^{II} \right] \right) \Big/ \left[Cd^{II} \right]_{ini} \right\}$$

$[Cd^{II}]_{ini}$: concentration of Cd^{II} in water before extraction; $[Cd^{II}]$: concentration of Cd^{II} in water after extraction.

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

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