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Novel Acyclic Polyethers Bearing Amide End-Groups and Their Complexation Studies in ISE

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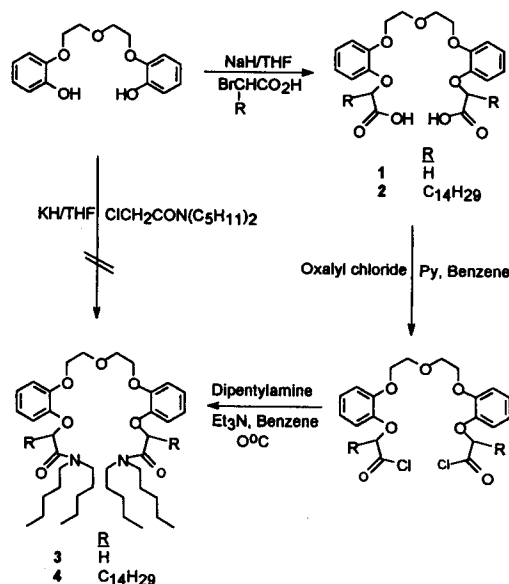
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Due to their complexation abilities with alkali, alkaline earth, and transition metals, a number of macrocyclic polyethers has been synthesized and employed for the separation of those metal ions.¹⁻³ Especially, complexation of metal ion with potential neutral chelating functions in the side arms have been well studied.⁴ Complexation studies with many natural ionophores such as valinomycin for potassium ion,⁵ monencin for sodium ion,⁶ and nonactin for ammonium ion⁷ have been well known. Potentiometric selectivities of solvent polymeric membrane electrodes containing structural derivatives of dibenzo-16-crown-5-oxyacetamides for sodium ion have been determined.⁸ Especially, selective separation of heavy metal ions such as Pb^{2+} and Cd^{2+} from industrial waste has long been considered as one of the most challenging problems remained in our environments.^{9,10} Therefore, much attention is now being paid to the recovery of and the detection of lead ion.

Complexation of acyclic dicarboxylic acid in which *n*-tetradecyl is replaced by *n*-hexyl group as a lipophilic side chain as denoted in Scheme 1 has shown an excellent selectivity for Pb^{2+} over Cu^{2+} in solvent extraction and in membrane transport experiment.¹¹ For solid state Pb^{2+} selective electrodes based on insoluble salts such as PbS , the presence of Cu^{2+} greatly interferes with the response of Pb^{2+} .¹² In addition,



Scheme 1. Synthetic Routes for the Preparation of Acyclic Polyether Amides **3** and **4**.

tion, several Pb^{2+} selective electrodes based on stannous hexacyanoferrate (III)¹³ and titanium arsenate¹⁴ have been reported and exhibited $\log K_{Pb,Cu}^{Pot}$ values of 0.4 and -1.5, respectively. Simon *et al.* reported a type of ionophore containing amide end-group which exhibits selectivities for $PbOH^+$, but poor selectivity for Pb^{2+} .¹⁵

Therefore, to enhance the selectivity for Pb^{2+} ion over other metal ions and to study the influence of nonionizable amide side arms and their lipophilicity on the complexation behavior by use of ISE system, herein we report that the synthetic methods for new compounds **3** and **4** which has pendant lipophilic side chains (*n*- $C_{14}H_{29}$) and results for the selective complexation of compound **3** and **4** with Pb^{2+} over other metal ions in ISE system.

Experimental

Chemical Analysis. IR spectra were obtained with a Perkin-Elmer 1600 Series FT-IR on potassium bromide pellet and are recorded in wave number. 1H NMR spectra were recorded with an AF-300 spectrometer with the chemical shifts (δ) reported downfield from the internal standard, tetramethylsilane. Elemental analysis was performed by Vario EL Elemental Analyzer in Korea Basic Science Institute in Seoul, Korea.

Chemicals. Unless specified otherwise, reagent grade reactants and solvents were obtained from chemical suppliers and used as received. Dry solvents were prepared as follows: benzene and pentane were stored over sodium ribbon; dichloromethane was freshly distilled from lithium aluminium hydride. 1,5-Bis[2-(carboxymethyloxy)phenoxy]-3-oxapentane (**1**) and 1,5-bis[2-(2'-carboxypentadecyloxy)phenoxy]-3-oxapentane (**2**) are known compound.¹⁶ Poly(vinyl chloride) (PVC) with an average polymerization degree of 1,100 was purchased from Waco Pure Chemical Industries. *o*-Nitrophenyloctyl ether (NPOE) and potassium tetrakis(*p*-chlorophenyl) borate (KTpClPB) were obtained from Dojindo Lab. Deioni-

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zed water was prepared by passing distilled water through an Organo G-10 cartridge.

Preparation of PVC Membranes. PVC (50 mg), NPOE (100 mg), the acyclic polyether diamide (5.0 mg), and KTpCIPB (1.0 mg) were dissolved in 1.5 mL of THF. The aliquot of THF solution was poured onto a porous poly(tetrafluoroethylene) (PTFE) membrane attached to a PVC tube, and the solvent was allowed to evaporate for 10-20 min. Addition of the THF solution and evaporation were repeated ten times. The resulting PVC tube with the coated PTFE membrane was fixed on a DKK No. 7900 (Denki Kagaku Keiki, Musashino, Tokyo, Japan) electrode body. An internal filling solution of 0.01 M PbCl_2 was added to the electrode.

Measurements. Potentiometric measurements with a membrane electrode were carried out at 24-25 °C with a voltage meter (Fisher Scientific Accumet 50 pH meter), a double-junction Ag-AgCl reference electrode (DKK No 4083), and a magnetic stirrer to agitate the sample solution. The electrode cell was Ag-AgCl/0.01 M PbCl_2 /PVC membrane/sample solution/0.01 M MgCl_2 /3 M KCl/Ag-AgCl.¹⁷ Selectivity coefficients ($K_{\text{Pb,M}}^{\text{Pot}}$) were determined by the fixed interference method.¹⁸

1,5-Bis[2-(N,N-dipentylacetamidooxy)phenoxy]-3-oxapentane (3). Under nitrogen, a solution of 1,5-bis[2-(carboxymethyloxy)phenoxy]-3-oxapentane (1) (2.00 g, 4.90 mmol), oxalyl chloride (4.27 mL, 49.0 mmol), and 1 drop of pyridine in 100 mL of dry benzene was refluxed for 10 h. The solvent and excess oxalyl chloride were removed *in vacuo*. To this crude product was added 50 mL of dichloromethane and 50 mL of water. Organic layer was separated, washed with 1 N HCl solution (2×50 mL) followed by drying over MgSO_4 . Removal of the solvent *in vacuo* gave a desired product 1,5-bis[2-(chloroacetyloxy)phenoxy]-3-oxapentane in quantitative yield as a yellowish oil. With spectroscopic evidences for the structural identification the obtained product was used without further purification. Under nitrogen, to a turbid solution of 1,5-bis[2-(chloroacetyloxy)phenoxy]-3-oxapentane (2.00 g, 4.90 mmol) and triethylamine (1.56 mL, 11.3 mmol) in 50 mL of dry benzene was added dropwise dipentylamine (2.39 mL, 11.3 mmol) during a period of 30 min at 0 °C. Upon the complete addition, the reaction mixture was stirred for additional 3 h at room temperature. Water (100 mL) was poured and organic layer was separated. Drying the benzene layer over MgSO_4 followed by filtration column chromatography of the residue on silica gel with ethyl acetate provided 3.20 g (96%) of desired product 3 as a colorless oil. IR (neat): 2929 (C-H); 1651 (C=O); 1254 (C-N) cm^{-1} . ^1H NMR (CDCl_3): δ 1.10-1.21 (2 t, $J=8.0$ Hz, 12 H); 3.37 (q, $J=7.9$ Hz, 8 H); 3.90-4.01 (m, 4 H); 4.15-4.23 (m, 4 H); 4.69 (s, 4 H); 6.92 (s, 8 H). Anal. calculated for $\text{C}_{40}\text{H}_{64}\text{O}_7\text{N}_2 \cdot 0.2$ *n*-hexane¹⁹: C, 70.47; H, 9.50. Found: C, 70.83; H, 9.50.

1,5-Bis[2-(2'-N,N-dipentylcarbamidopentadecyloxy)phenoxy]-3-oxapentane (4). Synthetic procedures for compound 4 from 1,5-bis[2-(2'-carboxypentadecyloxy)phenoxy]-3-oxapentane (2) is the same as that for compound 3. Colorless oil was obtained in 94% yield. IR (neat): 2921 (C-H); 1648 (C=O); 1254 (C-N) cm^{-1} . ^1H NMR (CDCl_3): δ 0.80-0.88 (m, 18 H); 1.16-1.67 (br s, 60 H); 1.73-2.08 (m, 4 H); 3.20-3.40 (m, 8 H); 3.91 (t, $J=7.4$ Hz, 4 H), 4.16 (t, $J=7.4$ Hz, 4 H); 4.78 (t, $J=7.4$ Hz, 2 H); 6.85-7.24 (m, 8 H). Anal.

calculated for $\text{C}_{68}\text{H}_{122}\text{O}_7\text{N}_2$: C, 75.64; H, 11.39. Found: C, 75.53; H, 11.20.

Results and Discussion

Synthesis of Acyclic Polyether Diamides. Synthetic routes for the preparation of acyclic polyether diamides are described in Scheme 1. Reaction of diphenol and bromoacetic acid or 2-bromohexadecanoic acid in THF by use of NaH as a base under nitrogen atmosphere provided desired products 1 and 2, respectively, with a good yield.¹⁶

Synthetic methods for N,N-dialkylamide from corresponding dicarboxylic acid were well known.²⁰ Also, it was reported that reaction of *sym*-(hydroxy)(propyl)dibenzo-16-crown-5 with KH in THF then with N,N-dipentyl 2-chloroacetamide as an alkylating agent gave a *sym*-(propyl)dibenzo-16-crown-5-oxacetamide with a quantitative yield.²¹ However, a number of attempts for the synthesis of compounds 3 and 4 with reported procedures^{20,21} including a direct coupling method of diphenol with N,N-dipentyl-2-chloroacetamide as depicted in Scheme 1 were unsuccessful. On the other hand, we found that a chlorination of dicarboxylic acid 1 and 2 with oxalyl chloride in the presence of catalytic amount of pyridine provides 1,5-bis[2-(chloroacetyloxy)phenoxy]-3-oxapentane and 1,5-bis[2-(2'-tetradecyl)chloroacetyloxy]phenoxy]-3-oxapentane were prepared in a quantitative yield as a yellowish oil, respectively. Upon the structural identification by spectroscopic analysis, the corresponding acid chloride was used in next reaction step without any further purification. Subsequently, reaction of corresponding acid chloride with dipentylamine and triethylamine as a base in benzene gave the compound 3 as a colorless oil. When the triethylamine was added, the reaction mixture immediately changed from transparent solution to turbid one. After dipentylamine was added dropwise, stirring the mixture for 1 h at room temperature gave a transparent brown solution which indicates the reaction finished.

Potentiometric Selectivities of Acyclic Polyether Diamides. The values of $\log K_{\text{Pb,M}}^{\text{Pot}}$ for compounds 3 and 4 are described in Figure 1. In response of ISEs based on the compound 3 to the change of Pb^{2+} activity, an average slope of 28.5 mv/decade was observed in the range of 1×10^{-3} - 1×10^{-6} M of sample solution. Potentiometric response to Pb^{2+} over other divalent metal ions showed an excellent selectivities with over at least 10^3 order in both compound 3 and 4. Compared with reported result which extraction coefficient of Pb^{2+} over Cu^{2+} showed 100-fold selectivity,¹¹ the $K_{\text{Pb,M}}^{\text{Pot}}$ value of compound 3 was less than -4.0 Even for Fe^{3+} , which greatly interferes with the measurement of solid-state ISEs based upon insoluble salts, the value of $\log K_{\text{Pb}^{2+},\text{Fe}^{3+}}^{\text{Pot}}$ is -3.4. However, compared with compound 3, attachment of tetradecyl side chain (compound 4) decreases the selectivity of Pb^{2+} over Cu^{2+} (-3.2) as well as over other metal ions. When the metal ion complexes with the ligand 4, the complexation may not be as easy as that with ligand 3. It is presumed that the extent of complexation in this system is controlled by a steric effect -two bulky $\text{C}_{14}\text{H}_{29}$ groups which are too long and large to form a pseudocyclic conformation with the metal ion- rather than by the lipophilicity concept.

In conclusion, syntheses of novel acyclic polyethers bearing

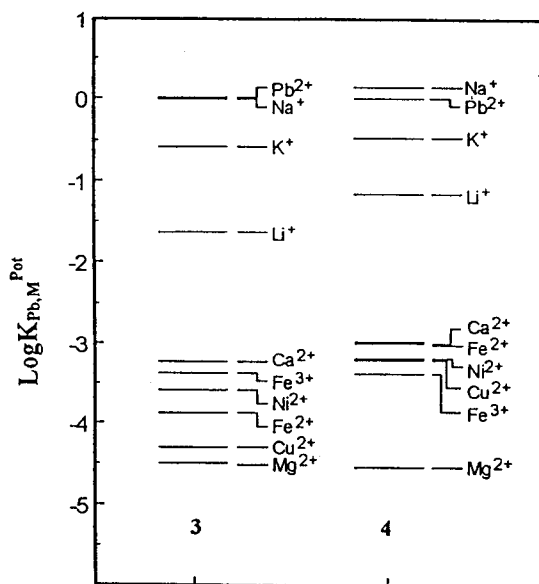


Figure 1. Potentiometric Selectivity of Compound 3 and 4 for Pb^{2+} over Other Metal Ions.

amide end-groups were successfully accomplished with quantitative yields. Complexation abilities of ligands 3 and 4 by ISE system show an excellent selectivity for Pb^{2+} over Cu^{2+} . To further investigate the influence of lipophilicity which decreases the $\text{Pb}^{2+}/\text{Cu}^{2+}$ selectivity in this study, syntheses of novel acyclic polyether diamides in which the length of lipophilic tail and the number of ethylene glycol units are varied and their complexation studies in ISEs are in progress and the results will be reported.

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Conformational Effects on the Palladium-Mediated Tandem Alkene Insertion Reactions

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Organopalladium chemistry has evolved as a powerful technique in organic synthesis.¹ Among them, palladium-promoted intramolecular² or intermolecular³ sequential alkene insertion reaction has recently attracted wide attention, because it constitutes a strong tool to form a series of C-C bonds in a single step. One of the strategies to achieve the Pd(0)-catalyzed tandem reaction is the intramolecular cycli-