

Syntheses and Potentiometric Properties of Polyethers Containing Thiazole and Oxazole Derivatives

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Received March 15, 1999

A series of polyethers containing the thiazole or oxazole subcyclic moiety have been synthesized. Reaction of 2-aryl-4-hydroxymethylthiazole with tetra- and pentaethylene glycol di-*p*-tosylate in THF provided corresponding α,ω -bis[2'-aryl-4'-methylthiazole]polyethylene glycol in good yields. Similar treatment of 2-phenyl-4-hydroxymethyloxazole **7** and 2-phenyl-5-hydroxymethyloxazole **8** with tetraethylene glycol di-*p*-tosylate yielded the corresponding 1,13-bis[2'-phenyl-4'-methylthiazole]tetraethylene glycol **16** and 1,13-bis[2'-phenyl-5'-methylthiazole]tetraethylene glycol **17** in 69 and 43% yields in respectively. The potentiometric properties of PVC-based ion selective membranes containing 66 wt% *o*-nitrophenyloctyl ether (NPOE) and 4 wt% polyethers **9-17** have been examined. The membranes containing thiazole and oxazole polyether derivatives exhibited high selectivity toward silver (I) ion. It was observed that the response slopes of the electrodes to silver ion vary with the length of polyether chain linking two thiazole subcyclic moiety. Potentiometric data suggest that the number of ether units, CH₂OCH₂, for phenylthiazole derivatives be greater than 5 to result in near-Nernstian response. However, the response behaviors of the membrane electrodes based on phenyloxazole podands **16** and **17**, which have different orientation, were correspondingly similar to those of the electrodes based on phenylthiazole podands **9** and **10**. On the other hand, the ISEs based on thiazole polyether derivatives with different terminal substituents, e.g., phenyl **10**, naphthyl **14**, and thienyl **15**, except that with pyridyl **12**, exhibited little difference in their potentiometric properties.

Introduction

Synthetic host molecules of abiotic origin such as crown ethers, cryptands, calixarenes, podands, and molecularly imprinted polymers have attracted considerable interests in all fields of chemistry as they are not only practically useful for separation and determination of specific guest molecules in complex matrix but also theoretically important models for realizing molecular recognition principles.¹ Those molecules are also often employed to construct highly selective chemical sensors.² Macrocyclic compounds containing heterocycle have been considered as one such class of host molecules for alkali, alkaline earth and transition metal cations, and intensively studied in the last decade. Although many macrocyclic compounds containing heterocycles, such as pyridine, bipyridine, pyrazole, and thiophene have been synthesized and studied,³ thiazole ring as a subunit of macrocyclic compounds has been known only in a few cases.⁴⁻⁶

Herein we report the synthesis of polyether podands that contain thiazole or oxazole. Also investigated were their potentiometric properties doped in solvent polymeric PVC membranes with respect to the length of polyether chain (CH₂OCH₂)_{*n*} and the type of terminal substituents, e.g., phenyl, naphthyl, thienyl and pyridyl group. We attempted to correlate the potentiometric selectivity and response behavior of various thiazole containing polyether derivatives with their structures.²

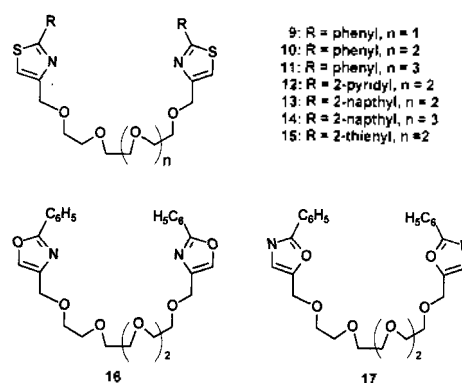


Figure 1

Experimental Section

General. Melting points were determined using a Thomas-Hoover capillary melting point apparatus and uncorrected. IR spectra were measured with a Galaxy FT-IR 7000 spectrophotometer and are reported in reciprocal centimeters. ¹H and ¹³C NMR spectra were obtained on a Varian Unity Plus 300 spectrometer as a solution in CDCl₃. The chemical shifts of ¹H NMR spectra (300.1 MHz) are reported in ppm (δ) relative to tetramethylsilane as the internal standard and ¹³C NMR (75.5 MHz) are referenced to CDCl₃ at 77.0 ppm. Mass spectra were recorded on a Shimadzu QP-100 spectrometer with electron energy of 20 or 70 eV. Elemental analyses were performed on a Calro Erba

1106 instrument. Analytical TLC analyses were performed on precoated 0.2 mm Merck Kieselgel 60F₂₅₄ plates, visualizing with a 254-nm UV lamp. Column chromatography was performed using Merck silica gel 70-230 mesh. All reactions were carried out under an atmosphere of argon. Solvent were dried and purified according to the known method.⁷ 2-Phenyl-4-carbethoxy-1,3-oxazole (**3**) was prepared by literature procedure.⁸ 1,10-bis[2'-phenyl-4'-methylthiazole] triethylene glycol (**9**), 1,13-bis[2'-phenyl-4'-methylthiazole]tetraethylene glycol (**10**), 1,16-bis[2'-phenyl-4'-methylthiazole]pentaethylene glycol (**11**), and 1,13-bis[2'-(2'-pyridyl)-4'-methylthiazole]tetraethylene glycol (**12**) were prepared following a reported procedure.⁵

Preparation of 2-Aryl-4-carbethoxythiazole.^{9,10} To a stirred solution of thioamide (1 mmol), BF₃ · Et₂O (0.25 mL, 2 mmol) in dry DME (5 mL) was added a solution of ethyl diazopyruvate (142 mg, 1 mmol) in dry DME (3 mL) for 2 h at room temperature and then the mixture was refluxed for 3h. The mixture was cooled to room temperature and then poured into water and extracted with ethyl acetate. The organic layer was washed with water, saturated solution of NaHCO₃ and brine, dried over anhydrous Na₂SO₄ and evaporated. The residue was purified by flash chromatography (silica gel, EtOAc/hexane 1 : 4) to give 2-aryl-4-carbethoxythiazole.

2-(2'-Naphthyl)-4-carbethoxythiazole (1). Yield 87%, white solid; mp 75.5-76 °C (CH₂Cl₂-hexane); TLC R_f 0.70 (EtOAc/hexane 1 : 2); IR (KBr) 3124, 2975, 1726, 1336, 1222, 1104, 746 cm⁻¹; ¹H NMR δ 8.51 (d, *J*=1.8 Hz, 1H), 8.19 (s, 1H, H-5), 8.10 (dd, *J*=8.4, 1.8 Hz, 1H), 7.89 (m, 3H), 7.54 (m, 2H), 4.50 (q, *J*=7.2 Hz, 2H, OCH₂CH₃), 1.45 (t, *J* = 7.2 Hz, 3H, OCH₂CH₃); ¹³C NMR δ 168.9 (C=O), 161.4 (C-2), 148.2 (C-4), 134.3, 133.1, 130.1, 128.8, 128.7, 127.8, 127.3, 127.1, 126.7, 126.6, 124.1, 61.5 (OCH₂CH₃), 14.4 (OCH₂CH₃); MS (*m/z*) 283 (M⁺, 95), 211 (100), 171 (73), 153 (26), 127 (22). Anal. Calcd for C₁₆H₁₃NO₂S: C, 67.83; H, 4.63; N, 4.95. Found: C, 67.84; H, 4.53; N, 4.52.

2-(2'-Thienyl)-4-carbethoxythiazole (2). Yield 84%, white solid; mp 70 °C (CH₂Cl₂-hexane); TLC R_f 0.33 (EtOAc/hexane 1 : 2); IR (KBr) 3071, 2973, 2906, 1723, 1464, 1335, 1206, 1094, 737 cm⁻¹; ¹H NMR δ 8.08 (s, 1H, H-5), 7.59 (dd, *J*=3.6, 1.2 Hz, 1H), 7.45 (dd, *J*=5.1, 1.2 Hz, 1H), 7.09 (dd, *J*=5.1, 3.9 Hz, 1H), 4.43 (q, 2H, OCH₂CH₃), 1.43 (t, *J*=7.2 Hz, 3H, OCH₂CH₃); ¹³C NMR δ 162.3 (C=O), 161.1 (C-2), 147.6 (C-4), 136.2, 128.7, 127.8, 127.6, 126.3 (C-5), 61.5 (OCH₂CH₃), 14.3 (OCH₂CH₃); MS (*m/z*) 239 (M⁺, 57), 167 (100), 111 (46), 46 (45).

2-Phenyl-5-carbethoxy-1,3-oxazole (4). To a stirred solution of rhodium (II) acetate (10 mg, 0.02 mmol) in 1 mL of benzonitrile was added a solution of ethyl diazopyruvate (138 mg, 1.0 mmol) in 4 mL of benzonitrile with syringe pump over 8 h period at 80 °C. After the reaction was completed, the solution was cooled and concentrated under high vacuum. The residue was purified by flash column chromatography (silica gel, EtOAc/hexane 1 : 4) to give 130 mg (60%) of **4** as a colorless solid, mp 65-66 °C (EtOAc-hexane); TLC R_f 0.47 (EtOAc/hexane 1:4); IR (KBr) 3005,

2985, 1711, 1312, 1150, 718 cm⁻¹; ¹H NMR δ 8.15 (m, 2H), 7.84 (s, 1H, H-4), 7.48 (m, 3H), 4.41 (q, 2H, *J*=6.9 Hz, OCH₂CH₃), 1.42 (t, 3H, *J*=6.9 Hz, OCH₂CH₃); ¹³C NMR δ 164.2 (C=O), 157.8, 142.3, 135.3, 131.6, 128.9, 127.2, 126.4, 61.5, 14.3; MS (*m/z*) 217 (M⁺, 46), 189 (21), 173 (3), 116 (100), 91(14).

Synthesis of 2-(2'-naphthyl)-4-hydroxymethylthiazole (5), 2-(2'-thienyl)-4-hydroxymethylthiazole (6), 2-phenyl-4-hydroxymethyl-1,3-oxazole (7) and 2-phenyl-5-hydroxymethyl-1,3-oxazole (8). To a suspension of lithium aluminum hydride (76 mg, 2 mmol) in THF (10 mL) was added 2-aryl-4-carbethoxythiazoles **5**, **6** or 2-phenyl-carbethoxyoxazoles **7**, **8** (2 mmol) at -78 °C. After the mixture was stirred at -78 °C for 2 h, the mixture was warmed to the room temperature and then ethyl acetate and water were added to the mixture. The mixture was washed with water and brine, dried over anhydrous Na₂SO₄ and evaporated. The residue was purified by column chromatography (silica gel, EtOAc/hexane 2 : 1) to give the corresponding products.

2-(2'-Naphthyl)-4-hydroxymethylthiazole (5). Yield 70%, white solid; mp 120 °C (CH₂Cl₂-hexane); TLC R_f 0.30 (EtOAc/hexane 1 : 1); IR (KBr) 3208, 3100, 3050, 2912, 2856, 1524, 1034, 1004, 823, 761 cm⁻¹; ¹H NMR δ 8.40 (s, 1H), 8.03 (dd, *J*=8.6, 1.7 Hz, 1H), 7.86 (m, 3H), 7.51 (m, 2H), 7.27 (s, 1H, H-5), 4.86 (d, *J*=6 Hz, 2H, CH₂OH), 2.74 (s, 1H, CH₂OH); ¹³C NMR δ 168.0 (C-2), 158.2 (C-4), 133.7, 132.8, 130.6, 128.4, 128.2, 127.5, 126.7, 126.5, 125.4, 123.7, 114.1 (C-5), 60.7 (CH₂OH); MS (*m/z*) 241 (M⁺, 100), 212 (30), 154 (42), 153 (46), 127 (28). Anal. Calcd for C₁₄H₁₁NOS: C, 69.69; H, 4.60; N, 5.81. Found: C, 69.74; H, 4.60; N, 5.34.

2-(2'-Thienyl)-4-hydroxymethylthiazole (6). Yield 71%, white solid; mp 92 °C (CH₂Cl₂-hexane); TLC R_f 0.23 (EtOAc/hexane 1 : 2); IR (KBr) 3211, 3073, 2921, 2851, 1532, 1412, 1029, 695 cm⁻¹; ¹H NMR δ 7.49 (d, *J*=3.3 Hz, 1H), 7.37 (d, *J*=5.4 Hz, 1H), 7.10 (s, 1H, H-5), 7.05 (m, 1H), 4.79 (s, 2H, CH₂OH), 3.50 (bs, 1H, CH₂OH); ¹³C NMR δ 162.3 (C-2), 156.9 (C-4), 136.9, 127.8, 127.7, 126.7, 113.9 (C-5), 60.7 (CH₂OH); MS (*m/z*) 197 (M⁺, 100), 168 (30), 110 (29).

2-Phenyl-4-hydroxymethyl-1,3-oxazole (7). Yield 76%, white solid; mp 70 °C (CH₂Cl₂-hexane); TLC R_f 0.41 (EtOAc/hexane 1 : 1); IR (KBr) 3241, 3111, 2920, 2870, 1551, 1483, 1352, 1030, 758, 689 cm⁻¹; ¹H NMR δ 8.03 (m, 2H), 7.64 (s, 1H, H-5), 7.45 (m, 3H), 4.69 (s, 2H, CH₂OH), 3.42 (bs, 1H, CH₂OH); ¹³C NMR δ 162.2 (C-2), 141.5 (C-4), 135.1 (C-5), 130.6, 128.8, 127.1, 126.4, 56.5 (CH₂OH); MS (*m/z*) 175 (M⁺, 81), 146 (24), 117 (42), 103 (100).

2-Phenyl-5-hydroxymethyl-1,3-oxazole (8). Yield 87%, white solid; mp 75 °C (CH₂Cl₂-hexane); TLC R_f 0.29 (EtOAc/hexane 1 : 1); IR (KBr) 3186, 2902, 2857, 1548, 1360, 1025, 708 cm⁻¹; ¹H NMR δ 7.95 (m, 2H), 7.39 (m, 3H), 6.99 (s, 1H, H-4), 4.67 (s, 2H, CH₂OH), 3.89 (bs, 1H, CH₂OH); ¹³C NMR δ 161.9 (C-2), 151.3 (C-5), 130.5, 128.7, 126.9, 126.2, 125.4 (C-4), 54.8 (CH₂OH); MS (*m/z*) 175 (M⁺, 69), 144 (66), 116 (100), 104 (50).

Synthesis of Thiazole-containing Polyethers 13-15 and

Oxazole-containing Polyethers 16-17. To a stirred mixture of potassium hydride (40 mg, 1 mmol), 2-aryl-4-hydroxymethylthiazoles **5**, **6** or hydroxymethylloxazole **7**, **8** (1 mmol) and THF (5 mL) was added a solution of tetraethylene glycol di-*p*-tosylate (0.5 mmol) in THF (10 mL) dropwise at 80 °C and the mixture was refluxed until the TLC (silica gel, 100% EtOAc) indicated the absence of starting material. The mixture was cooled to room temperature and poured into water and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous Na₂SO₄ and evaporated. The residue was purified by column chromatography (silica gel, EtOAc/hexane 3 : 1) to give the corresponding polyethers.

1,13-Bis[2'-(2'-naphthyl)-4'-methylthiazole]tetraethylene glycol (13). Yield 64%, colorless oil; TLC R_f 0.39 (EtOAc); IR (CHCl₃) 3104, 3055, 2870, 1451, 1352, 1107 cm⁻¹; ¹H NMR δ 8.41 (s, 2H), 8.03 (dd, *J*=8.6, 1.7 Hz, 2H), 7.86 (m, 6H), 7.50 (m, 4H), 7.30 (d, *J*=0.5 Hz, 2H, H-5), 4.78 (d, *J*=0.9 Hz, 4H, thiazole-CH₂), 3.80 (m, 4H), 3.73 (m, 4H), 3.66-3.69 (m, 8H); ¹³C NMR δ 168.3 (C-2), 155.2 (C-4), 134.1, 133.2, 131.0, 128.6, 128.6, 127.8, 126.9, 126.7, 125.9, 124.1 (C-5), 115.8, 70.6 (thiazole-CH₂OCH₂), 70.1, 69.8, 69.3; MS (*m/z*) 641 (M⁺+1, 1), 240 (85), 224 (100), 153 (25), 71 (35).

1,16-Bis[2'-(2'-naphthyl)-4'-methylthiazole]pentaethylene glycol (14). Yield 48%, colorless oil; TLC R_f 0.32 (EtOAc); IR (CHCl₃) 3061, 2891, 1453, 1360, 1113 cm⁻¹; ¹H NMR δ 8.42 (s, 2H), 8.04 (dd, *J*=8.0, 1.7 Hz, 2H), 7.85 (m, 6H), 7.50 (m, 4H), 7.31 (s, 2H, H-5), 4.78 (s, 4H, thiazole-CH₂), 3.79 (m, 4H), 3.72 (m, 4H), 3.70-3.57 (m, 12H); ¹³C NMR δ 168.4 (C-2), 155.2 (C-4), 134.1, 133.2, 131.0, 128.7, 128.6, 127.8, 126.9, 126.7, 125.9, 124.1 (C-5), 115.8, 70.7 (thiazole-CH₂OCH₂), 70.6, 70.2, 69.3; Fab. MS (*m/z*) 685 (M⁺+1), 447, 225, 154, 117.

1,13-Bis[2'-(2'-thienyl)-4'-methylthiazole]tetraethylene glycol (15). Yield 71 %, colorless oil; TLC R_f 0.20 (EtOAc); IR (CHCl₃) 3102, 2867, 1463, 1414, 1098 cm⁻¹; ¹H NMR δ 7.49 (d, *J* = 2.4 Hz, 2H), 7.37 (m, 2H), 7.20 (s, 2H, H-5), 7.06 (m, 2H), 4.71 (s, 4H, thiazole-CH₂), 3.78-3.68 (m, 16H); ¹³C NMR δ 161.8 (C-2), 154.6 (C-4), 137.2, 127.7, 127.5, 126.5, 114.8 (C-5), 70.6 (thiazole-CH₂), 70.6, 70.5, 70.1, 69.1; MS (*m/z*) 552 (M⁺, 3), 197 (90), 181 (100), 110 (23).

1,13-Bis[2'-phenyl-4'-methyloxazole]tetraethylene glycol (16). Yield 69%, colorless oil; TLC R_f 0.26 (EtOAc); IR (CHCl₃) 3131, 3065, 2915, 2870, 1555, 1096, 440 cm⁻¹; ¹H NMR δ 8.03 (m, 4H), 7.68 (s, 2H, H-5), 7.45 (m, 6H), 4.56 (s, 4H, oxazole-CH₂), 3.76-3.67 (m, 16H); ¹³C NMR δ 161.9 (C-2), 139.1 (C-4), 136.2 (C-5), 130.3, 128.7, 127.3, 126.4, 70.6 (oxazole-CH₂), 70.5, 70.5, 69.9, 65.2; MS (*m/z*) 509 (M⁺+1, 1), 332 (15), 174 (100), 158 (91), 130 (41), 103 (99).

1,13-Bis[2'-phenyl-5'-methyloxazole]tetraethylene glycol (17). Yield 43%, colorless oil; TLC R_f 0.20 (EtOAc); IR (CHCl₃) 3117, 3065, 2874, 1728, 1483, 1100, 795, 419 cm⁻¹; ¹H NMR δ 8.05 (m, 4), 7.44 (m, 6H), 7.14 (s, 2H, H-4), 4.61 (s, 4H, oxazole-CH₂), 3.67-3.64 (m, 16H); ¹³C NMR δ 161.9 (C-2), 148.4 (C-5), 130.2, 128.5, 127.3, 127.1, 126.2 (C-4),

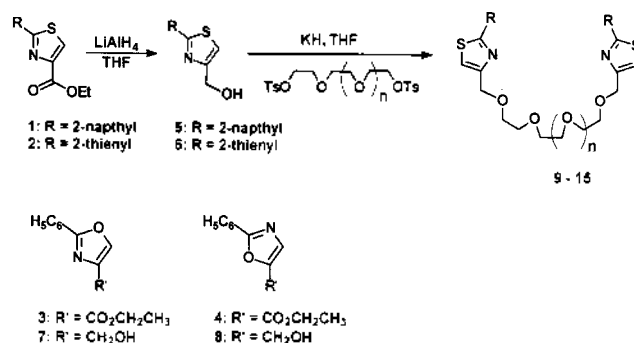
70.4 (oxazole-CH₂), 70.4, 70.3, 69.3, 62.6; MS (*m/z*) 508 (M⁺, 6), 174 (57), 158 (100), 104 (20), 89 (41).

Potentiometric Evaluation. The PVC-based membranes were normally prepared with 4 wt% ionophores (compounds **9-17** in Figure 1), 30 wt% PVC and 66 wt% plasticizer NPOE. These membrane components dissolved in 1 mL of THF were then poured into a glass ring (i.d. 18 mm) placed on a slide glass, and dried overnight at room temperature. Small disks were punched out from the cast films and mounted in Philips electrode bodies (IS-561; Glasblaserei Miller, Zrich, Switzerland).¹¹ For all electrodes, 0.1 M KCl was used as the internal reference electrolyte. The external reference electrode was an Orion sleeve-type double junction Ag/AgCl reference electrode (Model 90-02). Potential difference between the ISEs and the reference electrode was measured using an IBM AT-type computer equipped with a home made high-impedance input 16-channel analog-to-digital converter. The response curves were obtained by adding the standard solutions to the magnetically stirred background electrolyte (200 mL, 0.01 M magnesium acetate buffer, pH 4.5) every 100 seconds to vary the concentrations of primary ions (alkali, alkaline earth metal and various transition metal ions) stepwise from 10⁻⁷ to 10⁻³ M, and the measurements of *emf* values were taken every second at room temperature. Selectivity coefficients $k_{Ag^+,M}^{MPM}$ were estimated according to the separate solution-matched potential method at the 10⁻³ M ion concentration. It is known that this method appropriately describes the selectivity of ISEs that exhibit non-Nernstian response.¹²

Results and Discussion

Synthesis of Polyethers. Previous work on the reaction of ethyl diazopyruvate with thiobenzamide and 2-pyridinecarboxthioamide in the presence of 2 equiv of BF₃ · Et₂O in DME gives 2-phenyl-4-carbomethoxythiazole and 2-(2'-pyridyl)-4-carbomethoxythiazole in 82 and 41% yield in respectively.^{7,8} Similarly we could prepare 2-(2'-naphthyl)-4-carbomethoxythiazole **1**, 2-(2'-thienyl)-4-carbomethoxythiazole **2** from the reaction of the corresponding thioamide with ethyl diazopyruvate in the presence of BF₃ · etherate in DME in 87 and 84% yields, respectively.

The thiazole-containing polyethers were prepared as shown in Scheme 1. The transformation of the carbomethoxy



Scheme 1

Table 1. Synthesis of Polyethers

Compound	n	Yields(%) ^a
9	1	60 ^b
10	2	13 ^b
11	3	60 ^b
12	2	73 ^b
13	3	64
14	3	48
15	2	71
16	2	69
17	2	43

^aIsolated yield. ^bCited from reference 5.

group of compound **1** into hydroxymethyl group of compound **5** was carried out in 70% yield by reduction with LiAlH₄ at -78°C. Treatment of compound **5** with di-*p*-tosylates of the tetra and pentaethylene glycol in the presence of KH provided polyether **13** and **14** in 64 and 48% yields in respectively. (Table 1) The structures of compound **13** and **14** were confirmed by spectroscopic and analytical data. The molecular ion of **13** and **14** showed at 641 and 685 in mass spectrum. ¹H NMR of **13** showed one thiazole proton at δ 7.30 (s) and methylene protons adjacent to thiazole ring at δ 4.78 (d, *J*=0.9 Hz). Three thiazole carbons of **13** appeared at δ 168.3, 155.2 and 124.1 and methylene carbon adjacent to thiazole ring at δ 70.6 on ¹³C NMR. Compound **15** was prepared by an analogous sequence of steps starting with **2**. Reduction of **2** with LiAlH₄ at -78°C gave **6** in 71% yield, subsequent reaction of the latter with tetraethylene glycol di-*p*-tosylate resulted in 71% yield of **15**. The mass spectrum of **15** showed molecular ion at 552 (3% relative abundance). ¹H NMR of **15** showed three thiophene protons appeared at δ 7.49, 7.27 and 7.06 and one thiazole proton at δ 7.70.

The oxazole-containing polyethers were synthesized by similar treatment. Rhodium catalyzed reaction of ethyl diazopyruvate with benzonitrile provided 2-phenyl-5-carbethoxyoxazole **3** in 60% yield. 2-Phenyl-4-hydroxymethyloxazole **7** was prepared in 87% yield by treatment of ester **3** with LiAlH₄ in THF. Similar treatment of compound **4** with LiAlH₄ in THF provided 76% of 2-phenyl-5-hydroxymethyloxazole **8**. Reaction of compound **7** and **8** with tetraethylene glycol di-*p*-tosylate resulted in 69% yield of **16** and 43% of **17**. Most characteristic features of **17** involve the appearance of ¹H NMR signal at δ 7.14(s) assignable for the oxazole proton in addition to the ¹³C NMR peaks at δ 161.9, 148.4 and 126.2 for the C-2, C-5 and C-4 carbons. The molecular ion peak of **17** appeared at 508 (6% relative abundance) and its fragmentation is in accordance with the assigned structure.

Potentiometric Evaluation. Potentiometric properties of polyether derivatives **9-17** were examined with PVC membrane-based electrodes. First, the compounds **9-17** were classified into three groups for this purpose: compounds **9-11** by the number of ether unit, CH₂OCH₂, between two phenylthiazoles; compounds **10, 12, 13,** and **15** by the type of their substituted thiazoles and; compounds **16** and **17** by the

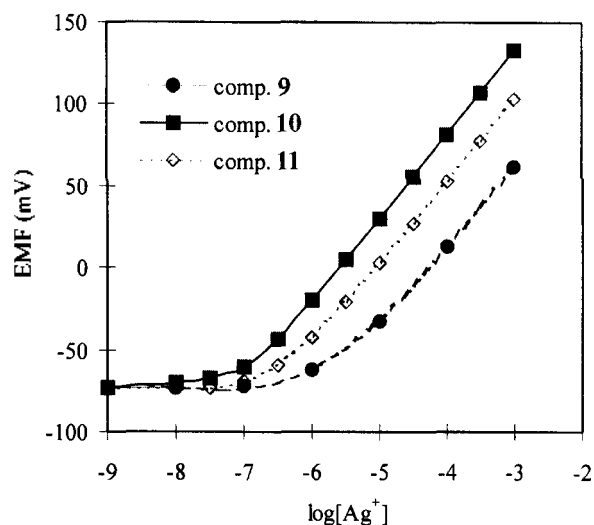


Figure 2. Potentiometric response curves for the PVC membrane electrodes based on phenylthiazole polyethers with different ether unit [(CH₂OCH₂)_n] to silver (I) ion: **9** (n=4), **10** (n=5), **11** (n=6). Background electrolyte: 0.01 M magnesium acetate/HNO₃, pH 4.5.

orientation of phenyloxazole.

Figure 2 compares the response curves for the electrodes based on first group of compounds. Of the three electrodes, the one based on compound **10** exhibits maximum response slope to Ag⁺ (51.5 mV/decade) with lower detection limit (d.l.=10⁻⁷ M). Since the detection limit of the membrane electrode is closely related to the complex formation constant of the ionophore doped in the membrane, higher detection limit (d.l.=10^{-6.5} M) and reduced response slope (41.7 mV/decade) of compound **9**-based electrode indicate that compound **9** form less tight silver complex than compounds **10** or **11** (d.l.=10^{-6.5}).¹³ As Table 2 shows, potentiometric selectivities of those electrodes to other metal cations (M) with respect to Ag⁺ (log k_{Ag⁺-M}^{MPM}) are negligible except to Hg²⁺. Considering that Ag⁺ tends to form AgL₂⁺ type linear complexes with ligand L and the thiazole nitrogen is a good binding site for silver ion,^{14,15} compounds **9-11** may chelate silver ion in the middle of two thiazole nitrogens, spiraling

Table 2. Matched Potential Selectivity Coefficients (log k_{Ag⁺-M}^{MPM}) of the PVC membrane electrodes based on Polyether derivatives **9-17** for various transition metal cations with respect to Silver (I) ion

Interferents	Compound								
	9	10	11	12	13	14	15	16	17
Ni ²⁺	-3.9	-4.2	<-5	-4.2	-4.2	-3.9	-3.6	-4.3	<-5
Zn ²⁺	-3.9	<-5	<-5	<-5	<-5	<-5	<-5	<-5	<-5
Co ²⁺	-4.0	<-5	<-5	-4.6	-5.0	<-5	<-5	<-5	<-5
Pb ²⁺	-3.7	-	-	-	-	-	-	-3.3	-3.1
Cd ²⁺	<-5	<-5	<-5	<-5	<-5	<-5	<-5	-4.8	<-5
Cu ²⁺	-4.0	-4.3	<-5	-3.0	-4.5	-4.5	<-5	-3.8	<-5
Fe ²⁺	-	-4.5	<-5	<-5	-4.4	-4.4	-	-3.9	-4.43
Hg ²⁺	-2.5	-2.6	-2.5	-2.3	-2.5	-2.5	-2.7	-2.4	-2.76
Slope ^a (mV/dec.)	41.7	51.2	48.7	38.7	46.2	47.9	47.7	35.6	49.16

^aValues determined in the 10⁻⁶ - 10⁻³ M range.

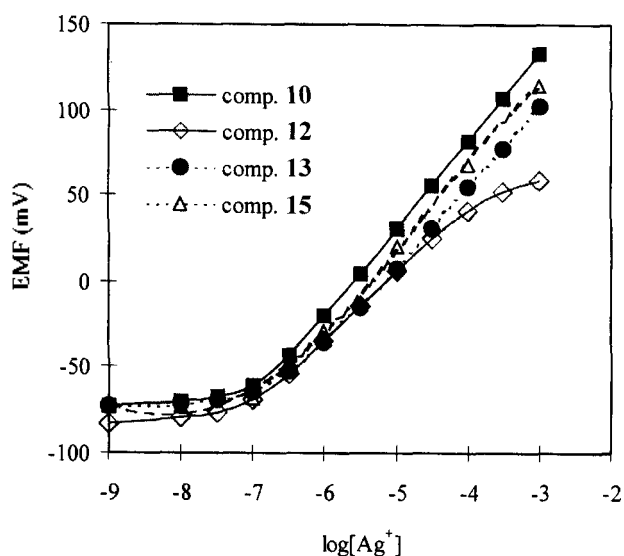


Figure 3. Potentiometric response curves for the PVC membrane electrodes based on polyether podands with different terminal substituents to silver (I) ion: phenylthiazole **10**, pyridylthiazole **12**, naphthylthiazole **13**, and thienylthiazole **15**. Background electrolyte: 0.01 M magnesium acetate/HNO₃, pH 4.5.

the polyether chain between them. If this were the case, optimal number of ether units may exist for binding silver cation. Figure 2 indicates that the number of ether unit between two phenylthiazoles be over 5 to result in near Nernstian response. As listed in Table 2, the experimental results for the electrodes based on naphthylthiazole derivatives with different length of polyether chain, i.e., compound **13** (5 ether units) and **14** (6 units), also support the same reasoning.

Figure 3 is the response curves for the electrodes based on second group of compounds. It is seen that the difference in their terminal substituents, i.e., phenyl-, naphthyl- and thienylthiazole of compound **10**, **13**, and **15**, respectively, cause relatively small change in the response slopes of the electrodes based on those compounds (see Table 2). On the other hand, the electrode based on pyridylthiazole derivative **12** resulted in reduced response slope (38.7 mV/decade). It has long been recognized that the reduced response at a higher cation concentration results from anionic interference.¹⁶ Recently, Bakker et al. showed that anion response of the silver-selective membrane occurs if the released free silver concentration at membrane-sample phase boundary decreases due to the formation of silver-anion precipitate.¹⁷ The release of silver ions from carrier-based silver-selective membrane is likely governed by the co-extraction of silver together with anionic impurity sites from the membrane. Thus, the experimental results indicate that compound **12** forms less tight silver complex than other second group compounds, allowing facile co-extraction of silver ion with anionic impurity sites from the PVC-based membrane.

Figure 4, the response curves for phenyloxazole derivative-based electrodes reveals another interesting feature as to the relationship between the orientation of oxazole and potentiometric response characteristics. It is seen that the

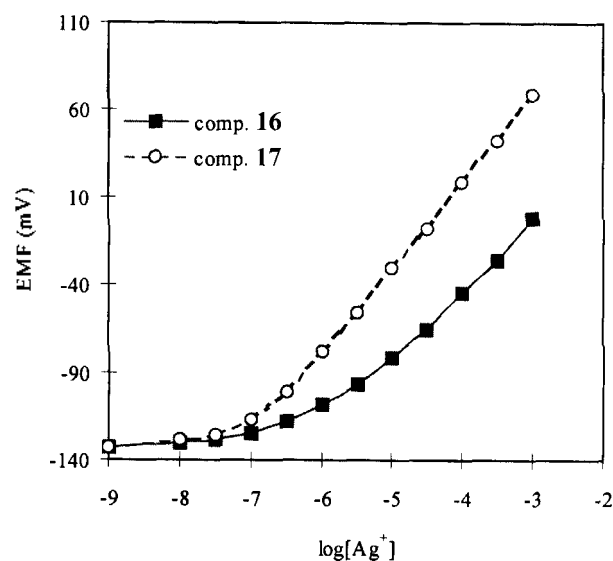


Figure 4. Potentiometric response curves for the PVC membrane electrodes based on phenyloxazole polyethers with different orientation to silver (I) ion: 2-phenyl-4-methyloxy-1,3-oxazole **16**, 2-phenyl-5-methyloxy-1,3-oxazole **17**. Background electrolyte: 0.01 M magnesium acetate/HNO₃, pH 4.5.

electrode based on 2,5-substituted oxazole **16** exhibits inferior potentiometric performance to that of the electrode based on 2,4-substituted compound **17**. A series of semi-empirical calculations with AM1 method indicates that the oxazole nitrogen is the primary cation binding site in compounds **16** and **17**. The model calculations showed that the bond lengths between oxazole nitrogen and a few cations (e.g., Na⁺, K⁺ and Hg⁺) examined are shorter by about 0.05 Å with compound **17** than with compound **16**, suggesting that the 2,4-substituted oxazole derivative is a favored cation-selective ionophore. However, this presumption is not thermodynamically supported as the differences in the heat of formation between the free and cation-complexed ionophore were almost same for both compounds. Apparently, the through the space long range interaction between the cation bound to oxazole nitrogen and ether oxygens makes the 2,5-substituted derivative-based membranes less responsive to cations.

Conclusion

A series of polyether derivatives with thiazole or oxazole subcyclic moiety has been synthesized to test their ionophoric ability. The plasticized PVC membranes doped with those compounds, in general, exhibited high selectivity toward silver ion. Experimental results and a series of semi-empirical calculations based on AM1 method indicate that the nitrogen in thiazole or oxazole ring is the main binding site for silver and other cations. The response slopes and detection limits of thiazole and oxazole compounds depend largely on the length of polyether chain, suggesting the possibility of forming 1 : 1 linear complex with silver by spiraling the polyether chain. On the other hand, it was observed that the difference in the type of terminal substituents (phenyl-

thiazole, naphthylthiazole and thienylthiazole) on both ends of polyether chain, except the ones with extra nitrogen like pyridyl group, has little effect on their potentiometric properties. These information may be used to design silver-selective ionophores of enhanced potentiometric properties.

Acknowledgment. This work was supported by the grant from the Basic Science Research Institute Program (1998-015-D00174) and the Center for Biofunctional Molecules.

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