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Synthesis and characterization of monoazathiacrown ethers as ionophores for polymeric membrane silver-selective electrodes

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ABSTRACT

Nine monoazathiacrown ethers have been synthesized and explored as ionophores for polymeric membrane Ag^+-selective electrodes. Potentiometric responses reveal that the ion-selective electrodes (ISEs) based on 2,2′-thiodiethanethiol derivatives can exhibit excellent selectivities toward Ag^+. The plasticized poly(vinyl chloride) membrane electrode using 22-membered N_2S_5-ligand as ionophore has been characterized and its logarithmic selectivity coefficients for Ag^+ over most of the interfering cations have been determined as <-8.0. Under optimal conditions, a lower detection limit of 2.2×10^{-10} M can be obtained for the membrane Ag^+-ISE.

1. Introduction

The development of chemical sensors for determination of heavy metals in the environment is of great importance from the ecotoxicological point of view [1]. For selective recognition, an efficient molecular receptor which has high potential as a complexing agent for a target heavy metal is required as sensing element [2]. Nowadays many compounds have been designed and synthesized to form remarkably stable and selective complexes with transition metal ions such as Schiffbases [3], podands [4], cyclams [5] and calixarenes [6]. Among them crown ethers containing nitrogen and sulfur donor atoms (i.e. azathiacrown ethers) are of special interest as they exhibit extremely high affinities toward heavy metal ions such as Ag^+, Hg^{2+} and Pb^{2+} [7–9]. Their selectivities and coordination abilities with transition metal ions depend on ring cavity size, ligand rigidity, the nature of donor atoms and their disposition [10]. In recent years, many azathiacrown ethers have been synthesized and successfully utilized for highly selective binding with heavy metals in diversal processes such as ion transports through artificial and natural membranes, liquid–liquid phase-transfer reactions and isotope separations [11–13].

Ion-selective electrodes (ISEs) are most frequently used potentiometric sensors for heavy metals due to high selectivity, good precision, low cost and simplicity. In recent years, the quest for improved lower detection limits of polymeric membrane ISEs has reinvigorated the search for better molecular receptors [2]. Several thiacrown ethers based on calixarenes have been explored as ionophores for heavy metals with lower detection limits [14,15]. However, so far there has been no report on the characterization of monoazathiacrown ethers as ionophores for the polymeric membrane ISEs with improved lower detection limits. In the present work, we have designed and synthesized nine monoazathiacrown ethers with different donor sites and ring sizes (Scheme 1). Potentiometric evaluation of the plasticized poly (vinyl chloride) membrane electrodes using those compounds as Ag^+-ionophores has been done in terms of their selectivity coefficients and detection limits for Ag^+.

2. Experimental

2.1. Reagents and instrumentation

Ethane-1,2-dithiol, 2,2′-thiodiethanethiol, poly (vinyl chloride) (PVC), benzene-1,2-dithiol, bis(2-ethylhexyl) sebacate (DOS), dibutylphthalate (DBP), dioctyl phthalate (DOP), 2-nitrophenyl octyl ether (*o*-NPOE) and sodium tetrakis [3,5-bis (trifluoromethyl)phenyl]borate (NaTFPB) were purchased from Sigma–Aldrich. All other reagents used were purchased from Sinopharm Chemical Reagent and of analytical grade purity or better. Deionized water with specific resistance of 18.2 MΩ cm was obtained by a Pall Cascada laboratory water system.

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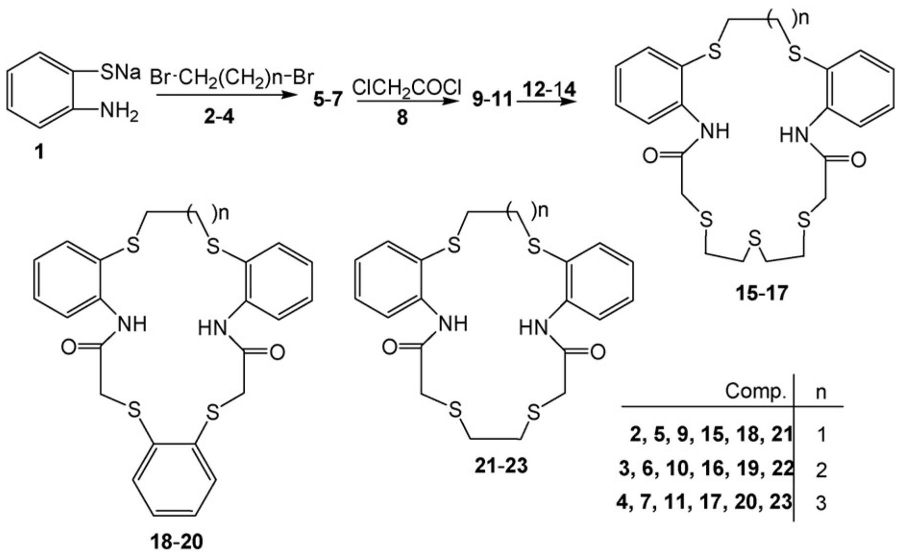

Scheme 1. Synthesis route for the macrocyclic compounds of **15–23**.

Melting points were measured with a WRS-1B digital melting-point apparatus (Shanghai, China). Infrared (IR) spectra were recorded on KBr pellets using a Perkin-Elmer 1430 spectrometer. Nuclear magnetic resonance (NMR) spectra were measured with a Brucker WM-300 spectrometer, and chemical shifts were given in ppm from tetramethylsilane. Mass spectra (MS) were recorded on a Thermo TSQ Quantum Mass Spectrometer. Elemental analyses were performed with a Vario III elemental analyzer.

*2.2. Synthesis of monoazathiacrown ethers **15–23***

*2.2.1. Synthesis of compounds **5–7***

General procedure. Compounds **5–7** were synthesized as described before [16,17]. 2-amino thiophenol 1 (1.25 g, 10 mmol) was added to sodium ethoxide which was formed by reaction of sodium (0.23 g, 10 mmol) with absolute ethanol (50 mL) under nitrogen atmosphere. A degassed solution of **2–4** (5 mmol) in absolute ethanol (20 mL) was added dropwise to the refluxing sodium thiophenolate solution with constant stirring. After the reaction was done, the resulting mixture was cooled to room temperature and filtered off, and the filtrate was poured into 300 mL cold water.

*2.2.1.1. 1,2-di(o-aminophenylthio)ethane **5**.* With the general procedure, the solid crude products obtained were recrystallized from ethanol, and a light grey residue was obtained, m.p. 76.1–76.9 °C (lit. 75 °C [16]); IR (KBr tablet, cm^{-1}): 3292.9 (N–H), 3059.5 (Ar-H), 1618.0 (C═C), 750.2 (C–S); ^{1}H NMR: (δ: ppm, $CDCl_3$): 7.31–7.33 (m, 2H, Ar-H), 7.10–7.14 (m, 2H, Ar-H), 6.70–6.72 (m, 2H, Ar-H), 6.64–6.68 (m, 2H, Ar-H), 4.34 (b, 4H, -NH_2), 2.86 (t, 4H, -CH_2-); MS m/z: 277.10 [M+1]$^+$.

*2.2.1.2. 1,3-di(o-aminophenylthio)propane **6**.* With the general procedure, the brown oil separated was extracted with diethyl ether. The ether was evaporated under reduced pressure. The oil product was dried with anhydrous Na_2SO_4 and used without further purification for the next step [17]. MS m/z: 291.08 [M+1]$^+$.

*2.2.1.3. 1,4-di(o-aminophenylthio)butane **7**.* With the procedure similar as that of **6**, the oil product obtained was used without further purification for the next step. MS m/z: 305.25 [M+1]$^+$.

*2.2.2. Synthesis of compounds (**9–11**)*

General procedure. A solution of chloroacetic anhydride **8** (50 mmol) in CH_2Cl_2 (50 mL) was added dropwise to a stirred solution of **5–7** (16 mmol) in CH_2Cl_2 (250 mL). The mixture was ice-bathed for 2 h and then stirred for 6 h under nitrogen atmosphere at room temperature. The resulting mixture was filtered off. Filtrate was washed with saturated aqueous $NaHCO_3$, and the organic layer was separated and removed under reduced pressure. The crude products were washed with ethanol and diethyl ether and dried in vacuum. The crude products were purified by recrystallization from acetonitrile to give compounds **9–11**.

*2.2.2.1. N,N′-{2,2′-[ethane-1,2-diylbis(sulfanediyl)]bis(2,1-phenylene)}bis(2-chloro-acetamide) **9**.* White crystals (65%); m.p. 167.8–168.2 °C; IR (KBr tablet, cm^{-1}): 3308.3 (N–H), 1679.7 (C═O), 1585.2, 1534.1, 1441.5, 1409.7, 769.4; ^{1}H NMR (δ: ppm, $CDCl_3$): 9.64 (s, 2H, NH), 8.40–8.42 (d, 2H, Ar-H), 8.45–8.47 (d, 2H, Ar-H), 7.36–7.40 (t, 2H, Ar-H), 7.06–7.10 (t, 2H, Ar-H), 4.22 (s, 4H, O═CCH_2Cl), 2.86 (s, 4H, SCH_2); ^{13}C NMR (δ: ppm, $CDCl_3$): 163.85 (C═O), 138.83, 135.61, 130.34, 124.99, 121.95, 120.13 (ArC), 43.37 (O═CCH_2S), 35.02 (SCH_2); MS: m/z 451.18 [M+Na]$^+$; Anal. Calcd. for $C_{18}S_2N_2Cl_2O_2H_{18}$ (429.38): C, 50.35; H, 4.23; N, 6.52. Found: C, 50.75; H, 4.30; N, 6.52.

*2.2.2.2. N,N′-{2,2′-[propane-1,3-diylbis(sulfanediyl)]bis(2,1-phenylene)}bis(2-chloro-acetamide) **10**.* White crystals (56%); m.p. 126.1–128.1 °C (lit. 131–132 °C [18]); IR (KBr tablet, cm^{-1}): 3319.9 (N–H), 1680.7 (C═O), 1581.3, 1527.3, 1435.7, 1402.0, 770.4; ^{1}H NMR (δ: ppm, $CDCl_3$): 9.71 (s, 2H, N–H), 8.40–8.42 (d, 2H, Ar-H), 7.34–7.38 (t, 2H, Ar-H), 7.05–7.09 (t, 2H, Ar-H), 4.23 (s, 4H, O═CCH_2Cl), 2.84–2.87 (t, 4H, SCH_2), 1.73–1.80 (m, 2H, $SCH_2CH_2CH_2S$).

*2.2.2.3. N,N′-{2,2′-[butane-1,4-diylbis(sulfanediyl)]bis(2,1-phenylene)}bis(2-chloro-acetamide) **11**.* White crystals (72%); m.p. 120.4–121.1 °C; IR (KBr tablet, cm^{-1}): 3285.1 (N–H), 1681.6 (C═O), 1581.3, 1520.2, 1443.5, 1406.8, 770.4; ^{1}H NMR (δ: ppm, $CDCl_3$): 9.71 (s, 2H, N–H), 8.39–8.41 (d, 2H, Ar-H), 7.49–7.51 (d, 2H, Ar-H), 7.33–7.37 (t, 2H, Ar-H), 7.07–7.11 (t, 2H, Ar-H), 4.23 (s, 4H, O═CCH_2Cl), 2.71–2.76 (t, 4H, SCH_2), 1.62–1.69 (m, 4H, SCH_2CH_2); ^{13}C NMR (δ: ppm, $CDCl_3$): 163.85 (C═O), 138.60, 135.35, 129.80, 124.83, 119.90, 77.00 (ArC), 43.34 ($ClCH_2$), 35.58 (SCH_2), 28.33 (SCH_2CH_2); MS: m/z 457.09[M]$^+$; Anal. Calcd. for $C_{20}S_2N_2O_2H_{22}Cl_2$

(457.44): C, 52.51; H, 4.83; N, 6.12. Found: C, 51.93; H, 4.65; N, 6.44.

*2.2.3. Synthesis of monoazathiacrown ethers **15–23***

General procedure. Monoazathiacrown ethers **15–22** were synthesized as described before [18]. A solution of **9–11** (0.5 mmol) in DMF (50 mL) and that of 2,2′-thiodiethanethiol (**12**), benzene-1,2-dithiol (**13**) or ethane-1,2-dithiol (**14**) (0.5 mmol) in DMF (50 mL) were added simultaneously to a solution of DMF (50 mL) containing 2 mmol anhydrous Na_2CO_3. The reaction was monitored by thin layer chromatography [petroleum ether–ethyl acetate (4:1)]. The whole process was operated under nitrogen atmosphere with vigorously stir for 1.5 h. The resulting mixture was filtered off and the solvent was removed under reduced pressure. The remaining residue was washed in turn with water, ethanol and diethyl ether and then dried in vacuum. The solid products were collected and crystallized from DMF to obtain pure compounds **15–23**.

*2.2.3.1. 9,10,12,13,15,17-hexahydrodibenzo[c,r][1,2,8,11,14,5,17]pentathiadiaza-cyclononadecine-6,16(5H,7H)-dione **15***

White crystals (89%); m.p. 185.0–186.4 °C; IR (KBr tablet, cm^{-1}): 3283.2 (N–H), 1660.3 (C=O), 1579.4, 1528.3, 1433.8, 746.3; ^1H NMR (δ: ppm, $CDCl_3$): 9.73 (s, 2H, N–H), 8.37–8.39 (d, 2H, Ar-H), 7.42–7.44 (d, 2H, Ar-H), 7.34–7.38 (t, 2H, Ar-H), 7.03–7.10 (t, 2H, Ar-H), 3.44 (s, 4H, $O{=}CCH_2$), 3.00 (s, 4H, $ArSCH_2$), 2.79–2.97 (m, 8H, S-H); ^{13}C NMR (δ: ppm, $CDCl_3$): 166.85 (C=O), 138.98, 134.63, 129.92, 124.72, 122.20, 120.56 (ArC), 38.25 (O=C–C), 35.13, 34.06, 32.13 (SCH_2); MS: *m*/*z* 511.14 $[M+1]^+$; Anal. Calcd. for $C_{22}S_5N_2O_2H_{26}$ (510.78): C, 51.73; H, 5.13; N, 5.48. Found: C, 51.96; H, 5.26; N, 5.72.

*2.2.3.2. 9,10,12,13,24,25-Hexahydro-5H,15H,23H-dibenzo[b,q][1,7,10,13,19,4,16]-pentathiadiazacyclodocosine-6,16(7H,17H)-dione **16***

White crystals; m.p. 173.5–173.9 °C (lit. 174–175 °C [18]); IR (KBr tablet, cm^{-1}): 3265.9 (N–H), 1672.9 (C=O), 1579.4, 1524.4, 1430.9, 1394.3, 764.6; ^1H NMR (δ: ppm, $CDCl_3$): 9.78 (s, 2H, NH), 8.33–8.35 (d, 2H, Ar-H), 7.35–7.47 (d, 2H, Ar-H), 7.31–7.35 (t, 2H, Ar-H), 7.06–7.10 (t, 2H, Ar-H), 3.45 (s, 4H, $O{=}CCH_2S$), 2.95–2.98 (t, 4H, SCH_2), 2.79–2.93 (m, 8H, SCH_2), 1.87–1.93 (m, 2H, $SCH_2CH_2CH_2S$); ^{13}C NMR (δ: ppm, $CDCl_3$): 166.74 (C=O), 138.71, 134.36, 129.49, 124.70, 123.34, 120.50 (ArC), 38.03 (O=C–C), 34.83, 34.04, 32.09 (SCH_2), 28.96; MS: *m*/*z* 547.10 $[M+Na]^+$; Anal. Calcd. for $C_{23}H_{28}N_2O_2S_5$ (524.80): C, 52.64; H, 5.38; N, 5.34. Found: C, 53.03; H, 5.46; N, 5.50.

*2.2.3.3. 9,10,12,13,15,17,23,24,25,26-decahydrodibenzo[b,q][1,7,10,13,19,4,16]-pentathiadiazacyclotricosine-6,16(5H,7H)-dione **17***

White crystals (92.3%); m.p. 180.3–181.0 °C; IR (KBr tablet, cm^{-1}): 3274.5 (N–H), 2920.7 (Ar-H), 1673.9 (C=O), 1578.4, 1521.6, 1430.0, 1406.8, 769.5; ^1H NMR (δ: ppm, $CDCl_3$): 9.61–9.71 (s, 2H, NH), 7.72–7.95 (d, 2H, Ar-H), 7.41–7.49 (d, 2H, Ar-H), 7.17–7.27 (t, 2H, Ar-H), 7.7.14–7.16 (t, 2H, Ar-H), 3.64 (s, 4H, $O{=}CCH_2S$), 2.98 (t, 4H, $ArSCH_2$), 2.82–2.88 (m, 4H, SCH_2), 2.50–2.73 (t, 4H, SCH_2), 1.58 (m, 4H, SCH_2CH_2); ^{13}C NMR (δ: ppm, $CDCl_3$): 167.68 (C=O), 137.60, 131.72, 128.00, 127.35, 125.45, 123.43 (ArC), 38.87 (O=C–C), 35.57, 33.46, 32.03 (SCH_2), 27.29; MS: *m*/*z* 539.1 $[M+1]^+$; Anal. Calcd. for $C_{24}S_5N_2O_2H_{30}$ (538.83): C, 53.50; H, 5.61; N, 5.20. Found: C, 52.47; H, 5.52; N, 5.15.

*2.2.3.4. 6,7,22,24-tetrahydrotribenzo[b,h,n][1,4,10,13,7,16]tetrathia-diazacycloocta-decine-14,23(13H,15H)-dione **18***

White crystals (98%); m.p. 222.5–224.5 °C; IR (KBr tablet, cm^{-1}): 3280.3 (N–H), 2922.4 (Ar-H), 1672.9 (C=O), 1578.4, 1519.6, 1436.7, 754.0; ^1H NMR (δ: ppm, $CDCl_3$): 9.88 (s, 2H, NH), 8.53–8.55 (d, 2H, Ar-H), 7.48–7.50 (d, 2H, Ar-H), 7.39–7.41 (d, 2H, Ar-H), 7.33–7.37 (t, 2H, Ar-H), 7.21–7.24 (t, 2H, Ar-H), 7.10–7.15 (t, 2H, Ar-H), 3.93 (s, 4H, $O{=}CCH_2$), 2.65–2.68 (t, 4H, SCH_2); ^{13}C NMR (δ: ppm, $CDCl_3$): 166.08 (C=O), 140.49, 135.82, 134.79, 130.53, 128.95, 128.01, 121.03, 119.73 (ArC), 38.54 (O=C–C), 36.92 (SCH_2); MS: *m*/*z* 521.02 $[M+Na]^+$; Anal. Calcd. for $C_{24}N_2O_2S_4H_{22}$ (498.70): C, 57.80; H, 4.45; N, 5.62. Found: C, 57.45; H, 4.52; N, 5.70.

*2.2.3.5. 6,7,14,15,16,22,23,24-octahydro-5H-tribenzo[b,h,n][1,7,10,16,4,13]tetrathia-diazacyclononadecine **19**.*

White crystals (94.5%); m.p. 220.9–221.3 °C; IR (KBr tablet, cm^{-1}): 3308.3 (N–H), 2962.1 (Ar-H), 1674.9 (C=O), 1578.4, 1518.7, 1439.6, 754.0; ^1H NMR (δ: ppm, $CDCl_3$): 10.05 (s, 2H, NH), 8.52–8.54 (d, 2H, Ar-H), 7.48–7.50 (d, 2H, Ar-H), 7.35–7.37 (t, 2H, Ar-H), 7.26 (d, 2H, Ar-H), 7.11–7.15 (t, 2H, Ar-H), 7.02–7.06 (t, 2H, Ar-H), 3.92 (s, 4H, $O{=}CCH_2$), 2.66–2.71 (t, 4H, SCH_2), 1.59–1.65 (m, 2H, SCH_2CH_2); ^{13}C NMR (δ: ppm, $CDCl_3$): 165.96 (C=O), 139.27, 134.67, 134.28, 130.16, 127.53, 127.46, 124.43, 122.57, 119.98 (ArC), 38.32 (O=C–C), 36.44, 31.39(SCH_2), 19.98 (CH_2); MS: *m*/*z* 535.04 $[M+Na]^+$; Anal. Calcd. for $C_{25}N_2O_2S_4H_{24}$ (512.73): C, 58.56; H, 4.72; N, 5.46. Found: C, 58.71; H, 4.82; N, 5.63.

*2.2.3.6. 14,16,22,23,24,25-hexahydrotribenzo[b,h,n][1,7,10,16,4,13] tetrathiadiaza-cycloicosine-6,15(5H,7H)-dione **20**.*

White crystals (95%); m.p. 201.2–203.0 °C; IR (KBr tablet, cm^{-1}): 3269.7 (N–H), 2920.7 (Ar-H), 1689.3 (C=O), 1577.5, 1518.7, 1438.6, 749.2; ^1H NMR (δ: ppm, $CDCl_3$): 9.93 (s, 2H, NH), 8.44–8.50 (d, 2H, Ar-H), 7.48–7.52 (d, 2H, Ar-H), 7.33–7.37 (t, 2H, Ar-H), 7.26–7.28 (d, 2H, Ar-H), 7.14–7.21 (t, 2H, Ar-H), 7.05–7.09 (t, 2H, Ar-H), 3.84–3.91 (s, 4H, $O{=}CCH_2$), 2.66 (t, 4H, SCH_2), 1.53–1.56 (m, 2H, SCH_2CH_2); ^{13}C NMR (δ: ppm, $CDCl_3$): 165.84 (C=O), 139.08, 134.99, 134.61, 129.61, 127.68, 127.51; 124.71; 123.78; 119.95 (ArC), 38.49 (O=C–C), 36.75, 27.71 (SCH_2), 16.84 (CH_2); MS: *m*/*z* 549.04 $[M+Na]^+$; Anal. Calcd. for $C_{26}N_2O_2S_4H_{26}$ (526.76): C, 59.28; H, 4.97; N, 5.32. Found: C, 59.24; H, 5.03; N, 5.32.

*2.2.3.7. 9,10,12,14,20,21-hexahydrodibenzo[e,q][1,4,10,13,7,16]tetrathiadiazacyclo-octadecine-6,13(5H,7H)-dione **21**.*

White crystals (90%), m.p.: 120.4–121.1 °C. IR (KBr tablet, cm^{-1}): 3291.9 (N–H), 2926.4 (Ar-H), 1667.2 (C=O), 1580.4, 1527.3, 1430.92, 768.5; Anal. Calcd. for $C_{20}S_4N_2O_2H_{22}$ (450.66): C, 53.3; H, 4.92; N, 6.22. Found: C, 53.44; H, 4.99; N, 6.33.

*2.2.3.8. 9,10,14,20,21,22-hexahydro-5H-dibenzo[b,n][1,7,10,16,4,13]tetrathiadiaza-cyclonon-adecine-6,13(7H, 12H)-dione **22**.*

White crystals (90.3%); m.p. 220.4–221.1 °C (lit. 222–223 °C [19]); IR (KBr tablet, cm^{-1}): 3282.2 (N–H), 2922.6 (Ar-H), 1664.3 (C=O), 1579.4, 1525.4, 1434.8, 767.5; ^1H NMR (δ: ppm, $CDCl_3$): 9.71 (s, 2H, N–H), 8.40–8.42 (d, 2H, Ar-H), 7.34–7.38 (t, 2H, Ar-H), 7.05–7.09 (t, 2H, Ar-H), 4.23 (s, 4H, $O{=}CCH_2Cl$), 2.84–2.87 (t, 4H, SCH_2), 1.73–1.80 (m, 2H, $SCH_2CH_2CH_2S$); MS: *m*/*z* 487.14 $[M+Na]^+$; Anal. Calcd. for $C_{21}S_4N_2O_2H_{24}$ (464.69): C, 54.28; H, 5.21; N, 6.03. Found: C, 54.44; H, 5.30; N, 6.08.

*2.2.3.9. 9,10,12,14,20,21,22,23-octahydrodibenzo[b,n][1,7,10,16,4,13]tetrathiadiaza-cycloicosine-6,13(5H,7H)-dione **23***

White crystals (94.2%); m.p. 217.5–218.3 °C; IR (KBr tablet, cm^{-1}): 3290.9 (N–H), 2919.7 (Ar-H), 1670.0 (C=O), 1579.4, 1521.6, 1435.7, 765.6; ^1H NMR (δ: ppm, $CDCl_3$): 9.73 (s, 2H, N–H), 8.38–8.40 (d, 2H, Ar-H), 7.50–7.52 (d, 2H, Ar-H), 7.34–7.38 (t, 2H, Ar-H), 7.09–7.12 (t, 2H, Ar-H), 4.22(s, 4H, $O{=}CCH_2$), 2.99 (t, 4H, $ArSCH_2$), 2.71–2.76 (t, 4H, SCH_2); ^{13}C NMR (δ: ppm, $CDCl_3$): 164.85 (C=O), 138.68, 134.35, 129.84, 124.63, 120.10, 77.13 (ArC), 38.34 (O=C–C), 35.58 ($ArSCH_2$), 33.23 (SCH_2); MS: *m*/*z* 501.10 $[M+Na]^+$; Anal. Calcd. for $C_{22}S_4N_2O_2H_{26}$ (478.71): C, 55.20; H, 5.47; N, 5.85. Found: C, 55.58; H, 5.54; N, 5.90.

2.3. Membrane preparation

The membranes were prepared with the newly synthesized ionophores **15–23** as described before [14]. The membrane components were dissolved in 3.0 mL of THF and shaken vigorously for at least 2 h, and then poured into a glass ring (30 mm i.d.) fixed on a glass plate. The solvent was allowed to evaporate overnight at room temperature to give a transparent membrane of 180 μm thickness. For each ISE, a disk of 7 mm diameter was punched from the membranes and glued to a plasticized PVC tube (i.d. 6 mm, o.d. 9 mm) with THF/PVC slurry. Electrodes for the lower detection limit detection were conditioned for 4 days in 10^{-5} $AgNO_3$ with 10^{-4} M NaCl/10^{-5} M $AgNO_3$ as inner solution. For long-term measurements, the electrodes were conditioned in 10^{-7} M $AgNO_3$.

2.4. Potential measurements

Activity coefficients were calculated according to the Debye–Hückel approximation and electromotive force (EMF) values were corrected for liquid-junction potentials with the Henderson equation. The reference electrode Hg/Hg_2Cl_2 with double junction was used with 1 M LiOAc as salt bridge electrolyte. Membrane potentials were measured with a Model PXSJ-216 digital ion analyzer (Shanghai Instruments) in magnetically stirred solution at room temperature in the galvanic cell:

SCE/1 M LiOAc/sample solution/ISE membrane/inner solution/AgCl/Ag

2.5. Selectivity measurements

The electrodes using 10^{-3} M NaCl as inner filling solution were conditioned in 10^{-2} M $NaNO_3$ overnight. Measurements were made in the respective nitrate solutions. The sequence of the sample ions was: Li^+, H^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Cu^{2+}, Cd^{2+}, Pb^{2+}, Hg^{2+} and Ag^+. For detection of Hg^{2+}, solutions were adjusted to pH 4 using 0.1 M HNO_3 to avoid precipitation. All the measurements were done in triplicate. The selectivity coefficients were calculated from the EMF values according to the separate solution method assuming theoretical slopes.

3. Results and discussion

The design and synthesis of mixed-donor crown ethers has been developing rapidly because of its applications in the field of coordination chemistry. Several synthetic methods have been developed [7], among which the high dilution method is most popular. The reactions proceed to give '1 + 1' macrocycles or '2 + 2' macrocycles depending on the chain length of starting materials [20]. In this work, a series of 18–23 membered azathiacrown ethers were synthesized in a simple route (Scheme 1). These nine monoazathiacrown ethers were explored as ionophores for polymeric membrane Ag^+-selective electrodes. The structure-selectivity relationship of the ionophore-based ISEs was also investigated.

3.1. Synthesis of ionophores

The reaction of the starting materials of **2–4** with the Na-salt of 2-amino thiophenol 1 in refluxing ethanol under nitrogen atmosphere produced the corresponding intermediates **5–7** in 70–75% yields [16,17]. As expected, the reaction of **5–7** with chloroacetylchloride **8** formed the compounds **9–11**. Subsequent cyclization of **9–11** with dithiol **12–14** in DMF in the presence of anhydrous Na_2CO_3 under nitrogen atmosphere at room temperature produced the corresponding macrocycles **15–23** in 83–95% yields, respectively. Data of compound structure analysis by MS, IR and NMR spectra are indicated in the Experimental Section. Indeed, the MS spectra data supported the formation of target compounds. The disappearance of aromatic primary-NH_2 vibration of compound **5–7** after introduction of amide function, and the presence of –NH and C=O groups stretching vibration at ~3300 and ~1680 cm^{-1}, respectively, confirm the proposed structures of compounds **9–11**. The IR spectra of macrocyclic compounds **15–23** are almost identical to those of compounds **9–11** [21]. In the ^{1}H NMR spectra of compounds **9–11**, the singlet at δ ~4.00 ppm corresponds to methylene protons between C=O and Cl groups. The protons of –NH group can be observed at δ ~9.73 ppm as a singlet. The C=O group of compounds **9–11** shows carbon response at δ ~163 ppm in the ^{13}C NMR spectra. The formation of macrocycles is confirmed by the appearance of SCH_2 protons at δ ~2.80 ppm in the ^{1}H NMR spectrum of compounds 18–20, 22–23 in $CDCl_3$.

Table 1
Compositions of the ISE membranes.

Membrane	Iono.	Iono. (wt%)	NaTFPB (wt%)	PVC (wt%)	Plasticizer (wt%)
A	**15**	0.70	0.30	33.0	66.0 (*o*-NPOE)
B	**16a**	0.70	0.30	33.0	66.1 (*o*-NPOE)
C	**16b**	0.46	0.54	33.0	66.0 (*o*-NPOE)
D	**16c**	0.64	0.36	33.0	66.0 (*o*-NPOE)
E	**16d**	0.71	0.29	33.0	66.1 (DOP)
F	**16e**	0.69	0.31	33.0	66.0 (DBP)
G	**16f**	0.70	0.31	33.2	65.7 (DOS)
H	**17**	0.70	0.30	33.0	66.0 (*o*-NPOE)
I	**18**	0.99	0.44	32.9	65.7 (*o*-NPOE)
J	**19**	1.0	0.43	32.9	65.7 (*o*-NPOE)
K	**20**	1.0	0.42	32.9	65.7 (*o*-NPOE)
L	**21**	0.68	0.32	33.0	66.0 (*o*-NPOE)
M	**22**	0.67	0.32	33.0	66.0 (*o*-NPOE)
N	**23**	0.69	0.31	33.0	66.0 (*o*-NPOE)

3.2. Characteristics of the ionophore-based Ag^+-ISEs

The selectivity coefficients, K^{pot}_{AgJ}, of Ag^+-ISEs were determined by using Bakker's method to eliminate the influence of the inherent sensitivity limit on the response toward discriminated ions [22]. The compositions of the membranes are listed in Table 1. The selectivity coefficients of all nine ionophores for Ag^+-ISE are shown in Table 2. It can be seen that all polymer membranes based on 2,2′-thiodiethanethiol derivatives **15–17** with five sulfur atoms as ionophores gave excellent K^{pot}_{AgJ} against the examined interfering ions as compared to other ionophores, although compound **16** with the ring number of 22 showed a little bit better selectivity toward Ag^+ than compounds **15** and **17**. These results are consistent with those reported previously showing that the selectivity of azathiacrown ethers to silver ions is proportional to the number of the sulfur atoms in the ring system [21,23]. It is interesting to note that the flexibility of the ring also has large effect on the selectivity

Table 2
Potentiometric selectivity coefficients, $\log K^{pot}_{AgJ}$, obtained with the separate solution method for *o*-NPOE-PVC (2:1) membranes based on ionophore **15–23**[a].

Ion J	$\log K^{pot}_{AgJ}$ [b]								
	15	**16a**	**17**	**18**	**19**	**20**	**21**	**22**	**23**
Li^+	−9.1	−10.2	−10.1	−6.9	−6.8	−7.0	−4.3	−3.1	−5.7
H^+	−8.3	−9.4	−9.4	−6.5	−6.2	−6.7	−3.9	−2.5	−5.4
Na^+	−8.2	−9.4	−9.1	−6.2	−5.9	−6.8	−3.4	−2.3	−5.1
K^+	−7.0	−8.2	−7.7	−4.7	−4.5	−5.1	−2.2	−0.9	−3.6
Mg^{2+}	−9.8	−10.8	−10.7	−7.6	−7.2	−7.8	−5.1	−3.5	−6.6
Ca^{2+}	−9.4	−10.1	−10.3	−7.2	−6.8	−7.4	−4.6	−3.3	−10.8
Cu^{2+}	−7.7	−9.0	−9.0	−7.5	−6.7	−7.5	−5.1	−3.6	−6.3
Cd^{2+}	−8.5	−10.0	−9.9	−7.9	−7.1	−8.0	−4.8	−3.6	−6.5
Pb^{2+}	−9.1	−8.4	−8.4	−6.4	−5.7	−6.1	−4.4	−2.6	−5.9
Hg^{2+}	−0.2	−2.5	−1.3	−0.5	−0.2	−0.6	−1.5	−0.2	0.5

[a] Inner filling solution: 10^{-3} M NaCl; conditioning solution: 10^{-2} M $NaNO_3$.
[b] Average value of three measurements.

Table 3
EMF responses of ISEs with ionophore 16 based on different plasticizers[a].

Plasticizers	EMF[b]/mV		ΔEMF/mV
	Blank	10^{-5} M Ag^+	
DOP	50.2 ± 0.3	130.6 ± 0.4	80.4
DBP	54.1 ± 0.7	444.5 ± 0.3	388.4
DOS	63.2 ± 0.4	437.0 ± 0.5	373.8
o-NPOE	25.1 ± 0.2	533.4 ± 0.3	508.3

[a] Inner filling solution: 10^{-3} M NaCl; conditioning solution: 10^{-2} M $NaNO_3$.
[b] Average value of three determinations ± standard deviation.

of ionophores. Atoms link with benzene group in which the carbon atoms have *SP*^{2} hybrid orbitals exist in the same planar with the benzene group. Such rigid structure makes it difficult for the ionophore to twist to form a stable complex with certain ions. Take ionophores 20 and 23 for example, both of them have the same ring members but different numbers of benzene groups. Ionophore 23 with less benzene groups is more flexible and could distort itself to give a suitable space to coordinate to Hg^{2+}. Indeed, the potentiometric response of the ISE based on ionophore 23 shows better response to Hg^{2+} than to Ag^+.

Experimental optimization of the Ag^+-ISE was investigated in terms of the composition of the ISE membrane. Since ionophores **15–17** exhibit improved potentiometric properties, i.e., low theoretical detection limit and high response slope, we characterized ionophore **16** with the best performance as Ag^+-ISE ionophore for the optimization. The polarity of the plasticizer influences the property of the electrodes. DOS and *o*-NPOE are representatives of low and high dielectric constant plasticizers with dielectric constants of 4.8 and 24, respectively, in their pure forms. *o*-NPOE plasticized PVC membranes have much higher polarities [24]. It can be seen in Table 3 that electrodes using *o*-NPOE as plasticizer show the best response. Furthermore, many studies have indicated that the ionic additives can improve the electrode response and for monovalent cations the optimal number of anionic sites is usually 50 mol% relative to the ionophore [25]. The results in Table 4 show that the amounts of the ionophore and NaTFPB in a molar ratio of 4:1 present the best results, which is consistent with the fact that compound **16** forms a sandwich complex with silver ion [18].

It have been fully realized that the primary ions leaching from the sensor membrane determine the lower detection limit of the measuring range of the ISEs [26]. One of the most common sources deteriorate the lower detection limit is due to the transmembrane fluxes of ions from the internal filling solution to the sample since the inner side contains a rather concentrated solution of the primary ions. Such fluxes can be reduced if primary ions in the inner filling solution are buffered with certain ligands, and thus, their concentration remains constant [27]. A number of different strategies via adjusting the concentration of inner solution have been reported [14,15,28,29]. Herein, we introduce an alternative approach using precipitation method according to the solubility product constant (K_{sp}) of AgCl to control the concentration of free Ag^+ in the inner solution. The response curves for ISEs with different inner solutions are shown in Fig. 1. For traditional ISE with 10^{-1} M $AgNO_3$ as inner solution, a concentration gradient from the inner solution toward the sample solution induces an enhanced primary ion concentration at the ISE membrane surface, so that lower detection limit cannot be achieved. On the other hand, the ISE conditioned in NaCl, with a strong flux of primary ions caused by the replacement of the primary ions in the membrane with the interfering ions (i.e., Na^+) due to ion exchange, exhibits the apparently super-Nernstian response in the range of 10^{-5} to 10^{-6} M, which could also deteriorate the lower detection limit. However, our experiments show that the lower detection limit can be improved when using NaCl/$AgNO_3$ mixture as inner solution. Indeed, the presence of Cl^- can lead to the precipitation of AgCl, thus decreasing the concentration of free Ag^+. For instance, the concentration of free Ag^+ in the inner solution of 10^{-5} M $AgNO_3$ with 10^{-4} M NaCl, calculated according to the solubility product constant (K_{sp}), is about 10^{-6} M. By using such precipitation buffer solution as inner solution of ISE, a concentration gradient of primary ions decreasing toward the inner solution can be built up, which could prevent the leaching of primary ions toward the sample solution and thus improve the detection limit. Detailed experiments have shown that the ISEs conditioned for 4 days in 10^{-5} M $AgNO_3$ with 10^{-5} M $AgNO_3/10^{-4}$ M NaCl as the inner solution can give the best potentiometric response. Under the optimal conditions, the electrode based on ionophore 16 shows the lower detection limit of 2.2×10^{-10} M Ag^+ and the near-Nernstian response slope of 54.5 mv per decade (Fig. 2). The electrode stability for long-term measurements was examined in the silver concentration range of 10^{-5} to 10^{-11} M. Experiments showed that no loss of potential response was observed after 25 days (Fig. 3).

Table 4
EMF responses of ISEs with ionophore 16 based on different ionophore : NaTFPB molar ratios[a].

Molar ratio	EMF[b]/mV		ΔEMF/mV
	Blank	10^{-5} M Ag^+	
2:1	64.8 ± 0.3	136.5 ± 0.4	71.7
3:1	54.2 ± 0.4	154.2 ± 0.5	100.0
4:1	25.1 ± 0.2	533.4 ± 0.3	508.3

[a] Inner filling solution: 10^{-3} M NaCl; conditioning solution: 10^{-2} M $NaNO_3$.
[b] Average value of three determinations ± standard deviation.

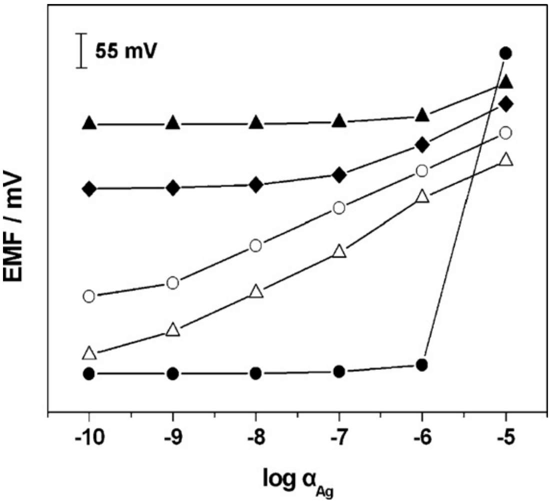

Fig. 1. Electrodes based on membrane B with different inner solutions: (▲) 10^{-1} M $AgNO_3$, (●) 10^{-3} M NaCl, (△) 10^{-3} M NaCl with 10^{-5} M $AgNO_3$, (○) 10^{-4} M NaCl with 10^{-5} M $AgNO_3$ and (♦) 10^{-5} M NaCl with 10^{-5} M $AgNO_3$.

4. Analytical applications

4.1. Titration of the mixture solution of Cl^-, Br^- and I^- ions

The proposed electrode (membrane B in Table 1) was used as an indicator electrode for the titration of the mixture of chloride, bromide and iodide ions. Due to the large difference between the K_{sp} values of AgI, AgBr, and AgCl, it is theoretically possible to potentiometrically titrate the mixture of iodide, bromide and chloride ions in one experiment [30]. Titration curves of the mixture of 2.0×10^{-3} M KI, KBr and KCl with 0.1 M $AgNO_3$ are illustrated in (Fig. 4). The endpoint of titration could be explicitly defined from

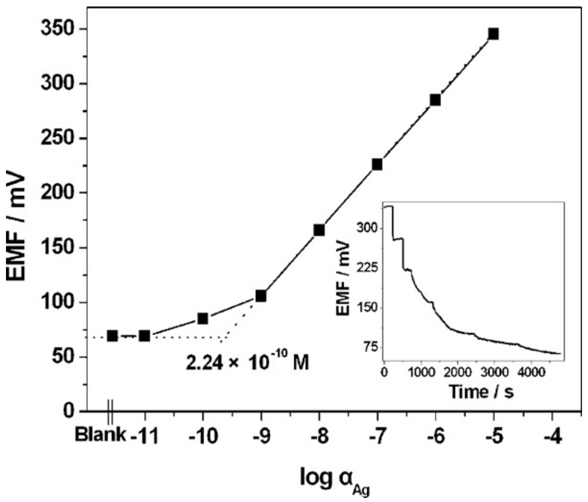

Fig. 2. Potentiometric response of the lower detection limit Ag$^+$-ISEs based on membrane B with 10^{-5} M $AgNO_3/10^{-4}$ M NaCl as inner solution. Inset shows the time-dependent EMF response trace of the Ag$^+$-ISE.

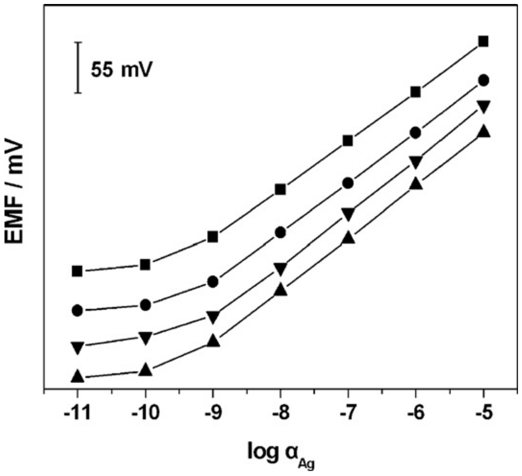

Fig. 3. Potentiometric responses of the Ag-ISE based on membrane B with 10^{-5} M $AgNO_3/10^{-4}$ M NaCl as inner solution after conditioned for different periods: (■) 4, (●) 11, (▼) 18 and (▲) 25 days.

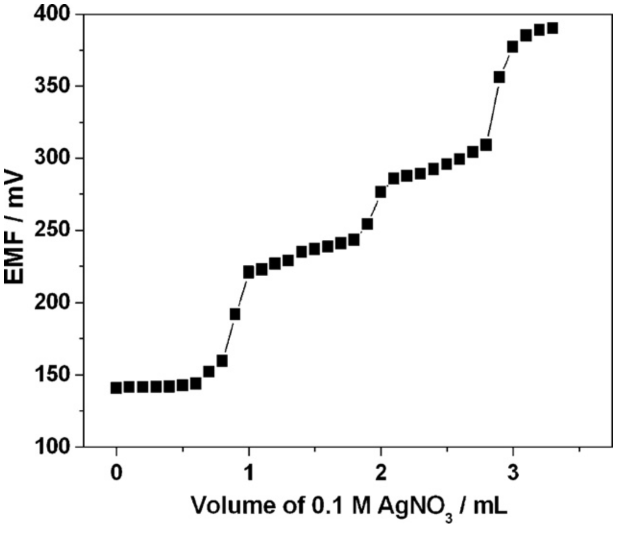

Fig. 4. Titration curve of the 50 mL mixture of chloride, bromide and iodine ions with 0.1 M Ag$^+$ as titration reagent obtained by using Ag$^+$-ISE based on membrane B with 10^{-5} M $AgNO_3/10^{-4}$ M NaCl as inner solution. The concentration of each ion was 2.0×10^{-3} M.

Table 5
Determination of Ag$^+$ in spiked tap water.

Sample	Added (nM)	Found[a] (nM)	Recovery (%)
Tap water 1	–	ND[b]	–
	20	19.8 ± 0.3	99
	30	30.3 ± 0.6	101
	60	62.2 ± 0.9	104
Tap water 2	–	ND[b]	–
	20	19.2 ± 0.4	96
	30	31.0 ± 0.3	103
	60	61.2 ± 0.6	102
Tap water 3	–	ND[b]	–
	20	19.8 ± 0.4	99
	30	30.5 ± 0.4	102
	60	61.0 ± 0.7	102

[a] Average value of three determinations ± standard deviation.
[b] Not detectable.

the titration curve by using $AgNO_3$ as the titrant. As can be seen, three end points are clearly established in the titration curve for each halogen. Therefore, the end-point and the amount of three halogen ions in a solution can be accurately potentiometrically determined by using this electrode.

4.2. Determination of Ag$^+$ in tap water

The Ag$^+$ concentrations in spiked tap water samples were determined by standard addition potentiometric method [31]. The results are shown in Table 5. It can be seen that the recoveries vary between 96% and 104%, thus indicating that the potential application of this proposed electrode could show high accuracy and good reliability for real water sample analysis.

5. Conclusions

Nine monoazathiacrown ethers have been synthesized and explored as ionophores for the construction of Ag$^+$-ISEs. The number of sulfur atoms is the decisive factor for the selectivity of Ag$^+$ as compared to the ring number and ring flexibility. The 22-membered N_2S_5-ligand has been successfully characterized as Ag$^+$ ionophore with a detection limit of 2.2×10^{-10} M. Using monoazathiacrown ethers as Ag$^+$-ionophore could open up a new way to design highly selective ionophores for Ag$^+$-ISEs with lower detection limits.

Acknowledgments

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