The Synthesis of Thiaazacrown Ethers Containing Pyridine as Subuint for the Construction of Ag⁺-ISEs

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Three new thiaazacrown ethers containing pyridine as subunit were synthesized and charaterized as Ag⁺-ion selective eslectrodes (Ag⁺-ISEs) ionophores. Study shows that the ring size and donor number of the ligands have great effect on the selectivity and sensitivity of the synthesized compounds. Potentiometric responses reveal that the ISE based on 2, 2'-thiodiethanethiol derivative exhibits best selectivity toward Ag⁺ relative to other two compounds. The plasticized poly (vinyl chloride) (PVC) membrane electrode using this N_3S_5-ligand as ionophore has been characterized in detail. Under optimal conditions, a detection limit of 3.9×10^{-7} M Ag⁺ can be obtained for the proposed membrane Ag⁺-ISE.

Keywords: Ion-selective electrode; Ag⁺; Thiaazacrown ether; Pyridine

1. INTRODUCTION

It is of great importance to develop chemical sensors for determination of heavy metals in the environment 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]. As powerful tools for separation, enrichment and analysis of ionic species, crown ethers have enjoyed widespread use in various areas of science and technology [3]. Since dithiacrown ethers were employed in the first neutral carrier-type Ag⁺-ISEs [4], thiaethers have been a very important class of ionophores for Ag⁺-ISEs [1-3, 5-9]. In the present work, three thiaazacrown ethers containing pyridine as subunit in high yields have been successfully synthesized (Scheme 1).

Potentiometric evalution of the plasticized PVC membrane electrodes using those compounds as Ag^+-ionophores has been done in terms of their selectivity coefficients and detection limits for Ag^+.
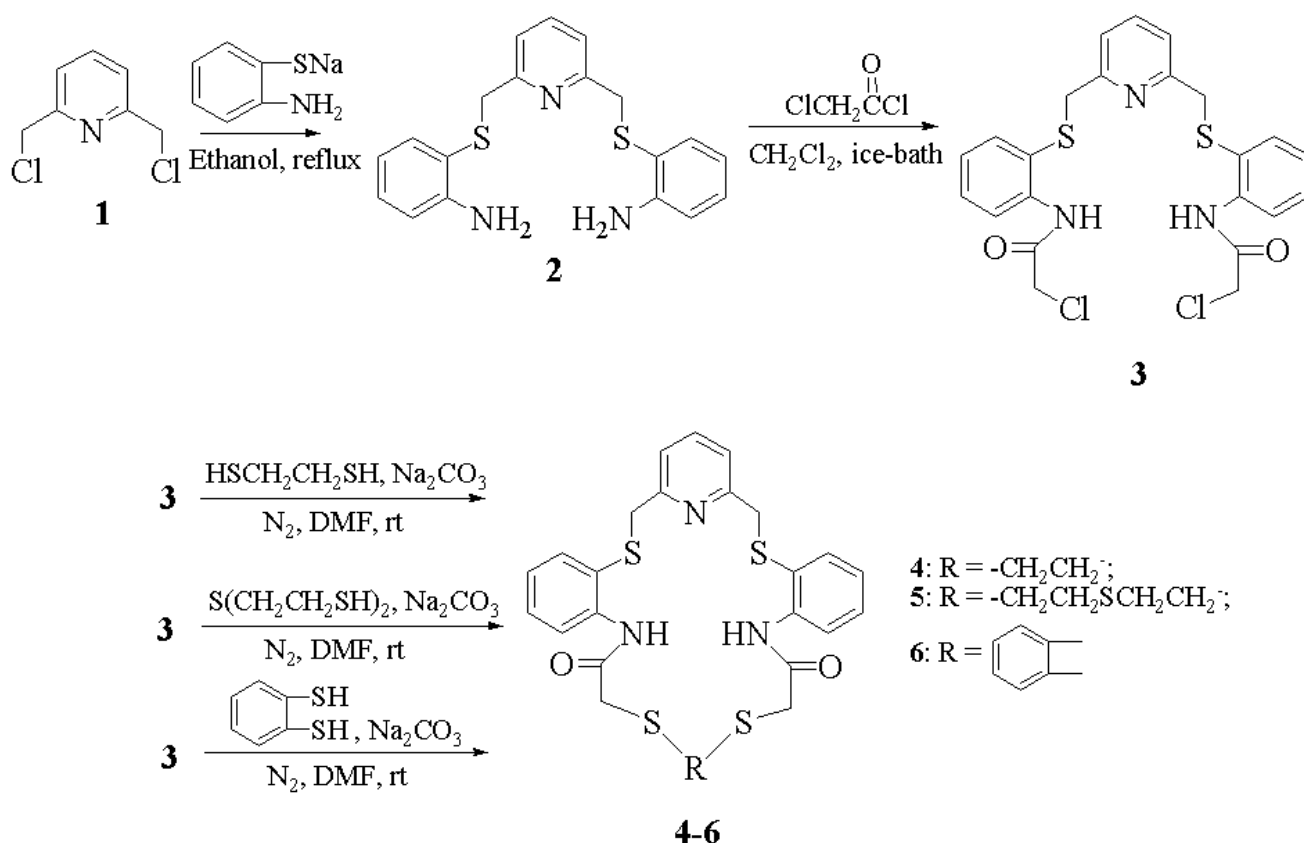
Scheme 1. The synthesis route of thiaazacrownethers **4-6**.

2. EXPERIMENTAL

2.1. Reagents and instrumentation

Ethane-1, 2-dithiol, benzene-1, 2-dithiol, 2, 2'-thiodiethanethiol, sodium tetrakis [3, 5-bis (trifluoromethyl)phenyl]borate (NaTFPB), PVC, 2-nitrophenyl octyl ether (NPOE), dioctyl phthalate (DOP), dibutylphthalate (DBP), bis(2-ethylhexyl) sebacate (DOS) 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.

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 thiaazacrown ethers *4-6*

2.2.1. Synthesis of compound *2*

2-amino thiophenol (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 **1** (5 mmol) in absolute ethanol (20 mL) was added dropwise to the refluxing sodium thiophenolate solution with 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. 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. ESI-MS, m/z: 354.22 $[M+1]^+$.

2.2.2. Synthesis of compound *3*

A solution of chloroacetic anhydride (50 mmol) in CH_2Cl_2 (50 mL) was added dropwise to a stirred solution of **2** (16 mmol) in CH_2Cl_2 (150 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, and filtrate was washed with saturated aqueous $NaHCO_3$. 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 compound **3** as white solid. Yields: 65.8%. ESI-MS, m/z: 506.29 $[M+1]^+$. ^{1}H NMR (δ: ppm, DMSO-d_6): 9.73 (s, 2H), 7.71 (t, 1H, *J*=7.72), 7.64 (d, 2H, *J*=7.90), 7.43 (d, 2H, *J*=9.15), 7.27 (t, 2H, *J*=8.37), 7.22 (d, 2H, *J*=7.75), 7.14 (t, 2H, *J*=8.15), 4.35 (s, 4H), 4.24 (s, 4H). ^{13}C NMR (δ: ppm, DMSO-d_6): 169.05, 165.38, 156.48, 139.19, 137.08, 131.97, 128.93, 128.12, 126.50, 124.82, 123.32, 122.71, 43.60, 41.96.

2.2.3. Synthesis of thiaazacrown ethers *4-6*

General procedure. A solution of **3** (0.5 mmol) in DMF (50 mL) and that of ethane-1, 2-dithiol or 2, 2'-thiodiethanethiol or benzene-1, 2-dithiol (0.5 mmol) in DMF (50 mL) were added simultaneously to a solution of DMF (50 mL) containing 2 mmol anhydrous Na_2CO_3 over 1.5 h. Then the whole process was operated under nitrogen atmosphere with vigorously stir for overnight at room temperature. The resulting mixture was filtered off and the solvent was treated with different methods according to the solubility of products.

Thiaazacrown ethers 4 and 5: The solvent was poured into 500 mL cold water and stirred, the white solid so produced was filtered and washed with water, ethanol and diethyl ether and then dried in vacuum.

Thiaazacrown ether 4: Yields: 94.1%. ESI-MS: m/z 528.14 $[M+1]^+$. ^{1}H NMR (δ: ppm, DMSO-d_6): 9.62 (s, 2H), 7.69 (d, 2H, *J*=7.60), 7.61 (t, 1H, *J*=7.70), 7.58 (d, 2H, *J*=9.25), 7.27 (t, 2H, *J*=8.35),

7.17 (d, 4H, *J*=7.55), 4.21 (s, 4H), 3.40 (s, 4H), 2.94 (t, 4H, *J*=7.50). (For the poor solubility, only H-spectrum was obtained).

Thiaazacrown ether **5**: Yields: 92.3%. ESI-MS: m/z 588.17 [M+1]$^+$. ^{1}H NMR (δ: ppm, DMSO-*d₆*): 9.59 (s, 2H), 7.73 (d, 2H, *J*=8.00), 7.61 (t, 1H, *J*=7.70), 7.51 (d, 2H, *J*=9.15), 7.27 (t, 2H, *J*=8.30), 7.14 (m, 4H), 4.18 (s, 4H), 3.41 (s, 4H), 2.82 (t, 4H, *J*=8.47), 2.73 (t, 4H, *J*=7.05). ^{13}C NMR (δ: ppm, DMSO-*d₆*): 168.23, 157.00, 138.01, 137.73, 132.67, 128.32, 128.26, 125.87, 123.86, 122.13, 41.19, 37.70, 36.77, 31.71.

Thiaazacrown ether **6**: The solvent was removed under reduced pressure. The remaining white residue was washed in turn with water, ethanol and diethyl ether, and then dried in vacuum. Yields: 89.5%. ESI-MS: m/z 576.16 [M+1]$^+$. ^{1}H NMR (δ: ppm, DMSO-*d₆*): 9.52 (s, 2H), 7.83 (d, 2H, *J*=7.90), 7.57 (t, 1H, *J*=8.85), 7.51 (t, 1H, *J*=7.67), 7.39 (d, 2H, *J*=8.65), 7.29 (t, 2H, *J*=8.17), 7.17 (d, 3H, *J*=8.90), 7.14 (t, 1H, *J*=7.00), 6.97 (d, 2H, *J*=7.65), 4.10 (s, 4H), 3.91 (s, 4H). ^{13}C NMR (δ: ppm, DMSO-*d₆*): 166.92, 162.82, 156.80, 138.34, 137.63, 135.52, 133.45, 129.13, 128.73, 127.56, 127.08, 125.77, 123.02, 122.19, 35.91, 32.67, 31.19.

2.3. Membrane preparation

The membrane components (totaling mass of 250 mg) were dissolved in 3.0 mL of THF and shaken vigorously at least 3 h, and then poured into a glass ring (30 mm i.d.) fixed on a glass plate and covered with a big beaker. The solvent was allowed to evaporate overnight at room temperature to give a transparent membrane (thickness 180 μm), and the resulting membrane was cut to size (7 mm i.d.) and glued with a PVC/THF slurry on the top of PVC tube mechanically fixed onto a pipette tip. The tube was then flled with inner flling solution (0.1 M AgNO$_3$) and conditioned for 1 d in 1.0×10^{-3} M AgNO$_3$.

2.4 EMF measurements

The polymeric membrane electrodes were conditioned overnight. Activity coefficients were calculated according to the Debye–Hückel approximation and EMF values were corrected for liquid-junction potentials with the Henderson equation. The reference electrode Hg/Hg$_2$Cl$_2$ (SCE) with double junction was used with 1.0 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 (25 °C) in the galvanic cell:

Ag, AgCl|Inner solution|PVC membrane|Sample solution ‖1.0 M LiOAc|SCE

2.5 Selectivity measurements

An electrode with 1.0×10^{-3} M NaCl as an inner filling solution was conditioned in 1.0×10^{-2} M NaNO$_3$ solution overnight. The response of the electrode was first measured against the interfering metal ions (1.0×10^{-6} to 1.0 M). The electrode was then used to measure the response of silver nitrate

solutions. The measurement was done in triplicate (using new membrane for one replicate). The interfering ions studied here were H^+, Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Cu^{2+}, Cd^{2+}, Pb^{2+} and Hg^{2+}. For determination of the selectivity coefficient of Hg^{2+}, the solution pH was adjusted to pH 4 using 0.1 M HNO_3.

3. RESULTS AND DISCUSSION

3.1 Effect of NaTFPB

Ionic additive can not only reduce the ohmic resistance but also improve the response behavior and selectivity as well as reduce anion interference [1, 5-7]. In this work, the effect of NaTFPB as ionic additive on the response of the silver electrodes was studied. The amount of NaTFPB was altered while maintaining the same amounts of PVC and plasticizer (NPOE) in the membranes (Table 1). The results show that the electrode based on ionophores **4-6** and NaTFPB in a mole ratio of 4:1 present the best potential responses, which indicates that compound **4-6** form complex with Ag^+ in a mole ratio of 2:1 in membrane phase.

Table 1. Influence of the amount of NaTFPB on the characteristics of Ag^+-ISEs.

Sensor No.	Compositions of membrane, w%				Working range, M	Detection limit, M	Slope, mV/dec.
	Iono.	NaTFPB	PVC	Plasticizer			
4a	0.54	0.46	33.0	66.0, NPOE	1.0×10^{-5}–1.0×10^{-3}	6.5×10^{-6}	48.2
4b	0.70	0.30	33.0	66.0, NPOE	3.0×10^{-6}–3.0×10^{-3}	1.2×10^{-6}	52.7
5a	0.57	0.43	33.0	66.0, NPOE	1.0×10^{-6}–1.0×10^{-3}	7.6×10^{-7}	49.3
5b	0.73	0.27	33.0	66.0, NPOE	1.0×10^{-6}-3.0×10^{-3}	3.9×10^{-7}	55.8
6a	0.57	0.43	33.0	66.0, NPOE	3.0×10^{-5}–1.0×10^{-2}	2.5×10^{-5}	51.2
6b	0.72	0.28	33.0	66.0, NPOE	3.0×10^{-6}–1.0×10^{-3}	1.7×10^{-6}	54.6

### 3.2 Effect of solvent mediators

Plasticizers show effect on the migration rate of carrier and ion, thus affect the balance time between the carrier and ion in the membrane phase. And the plasticizers also play an important role on the sensitivity and selectivity of the electrodes. The influences of plasticizers on the properties of ISEs mainly depend on the dielectric constant of different plasitizers [1, 9, 10-13]. In this work, electrodes with thiaazacrown ethers **4-6** as ionophores using different solvent mediators, NPOE ($\varepsilon_r=24.0$), DOS ($\varepsilon_r=4.8$), DBP ($\varepsilon_r=6.42$) and DOP ($\varepsilon_r=5.0$) were prepared. The response characteristics of these electrodes are given in Table 2. From Table 2 one can see that the electrode with NPOE as the solvent mediator shows obvious better response performance for Ag^+ comparing to other solvent mediators with a lower detection limit. It might be NPOE plasticized PVC membranes have much higher dielectric constants caused by better dielectric characteristics of NPOE comparing to other solvents,

which is favourable for response performance. Ag$^+$-ISE based on compound **5** gave the best potentiometric responses, and with optimal membrane composition, the new Ag$^+$-ISE shows a wide working range from 1.0×10^{-6} to 3.0×10^{-3} with a low detection limit of 3.9×10^{-7} M Ag$^+$ (Fig. 1).

Table 2. Influence of the nature of plasticizers on the characteristics of Ag$^+$-ISEs.

Sensor No.	Compositions of membrane, w%				Working range, M	Detection limit, M	Slope, mV/dec.
	Iono.	NaTFPB	PVC	Plasticizer			
4b	0.70	0.30	33.0	66.0, NPOE	3.0×10^{-6}–3.0×10^{-3}	1.2×10^{-6}	52.7
4c	0.70	0.30	33.0	66.0, DOS	1.0×10^{-5}–3.0×10^{-3}	8.2×10^{-6}	54.7
4d	0.70	0.30	33.0	66.0, DBP	3.0×10^{-6}–1.0×10^{-3}	1.6×10^{-6}	49.3
4e	0.70	0.30	33.0	66.0, DOP	1.0×10^{-5}–1.0×10^{-2}	2.5×10^{-6}	54.2
5b	0.73	0.27	33.0	66.0, NPOE	1.0×10^{-6}-3.0×10^{-3}	3.9×10^{-7}	55.8
5c	0.73	0.27	33.0	66.0, DOS	1.0×10^{-5}-1.0×10^{-3}	3.9×10^{-6}	52.5
5d	0.73	0.27	33.0	66.0, DBP	3.0×10^{-6}–1.0×10^{-2}	1.4×10^{-6}	53.1
5e	0.73	0.27	33.0	66.0, DOP	3.0×10^{-6}–1.0×10^{-3}	9.5×10^{-7}	54.7
6b	0.72	0.28	33.0	66.0, NPOE	3.0×10^{-6}–1.0×10^{-3}	1.7×10^{-6}	54.6
6c	0.72	0.28	33.0	66.0, DOS	1.0×10^{-5}–1.0×10^{-2}	6.8×10^{-6}	54.2
6d	0.72	0.28	33.0	66.0, DBP	3.0×10^{-6}–1.0×10^{-3}	1.2×10^{-6}	44.7
6e	0.72	0.28	33.0	66.0, DOP	1.0×10^{-5}–1.0×10^{-3}	5.5×10^{-6}	51.2
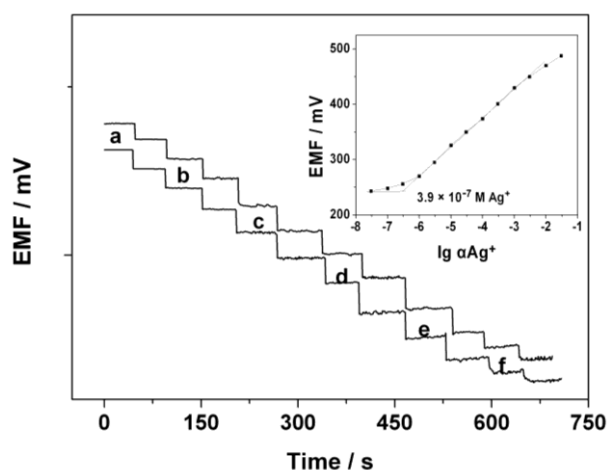
Figure 1. Time-dependent EMF responses of the Ag$^+$-ISE (Sensor No. **5b**): a. 3.0×10^{-2}, b. 3.0×10^{-3}, c. 3.0×10^{-4}, d. 3.0×10^{-5}, e. 3.0×10^{-6}, f. 3.0×10^{-7} M. Insert shows the detection limit and the working range of the proposed Ag$^+$-ISE.

3.3 Selectivity

Selectivity of an ionophore is the most crucial characteristic of an ISE [8, 14-16]. The ionophore should have good selectivity over interfering ions in order to avoid the bias response from such interfering ions. The selectivity of the ionophore results from the complex formation between the

ionophore and an analyte ion. The selectivity of ISE's was explored based on the so-called "unbiased selectivity coefficient" proposed by Bakker and co-workers [16].

Table 3. Potentiometric selectivity coefficients, $\log K_{AgJ}^{pot}$, obtained with the separate solution method for NPOE-PVC (2:1) membranes based on ionophore **4-6**[a].

Ion J	$\log K_{AgJ}^{pot}$ [b]		
	4	5	6
Ag^+	0	0	0
Li^+	-5.93	-7.23	-5.67
H^+	-5.47	-7.36	-5.12
Na^+	-5.19	-7.11	-4.26
K^+	-4.74	-5.47	-3.19
Mg^{2+}	-5.62	-8.26	-4.62
Ca^{2+}	-5.17	-8.20	-4.82
Cu^{2+}	-5.54	-7.35	-4.54
Cd^{2+}	-5.91	-7.72	-4.38
Pb^{2+}	-4.44	-6.32	-3.47
Hg^{2+}	-0.12	-0.34	-0.23

[a] Inner filling solution: 1.0×10^{-3} M NaCl; conditioning solution: 1.0×10^{-2} M NaNO$_3$.
[b] Average value of three measurements.
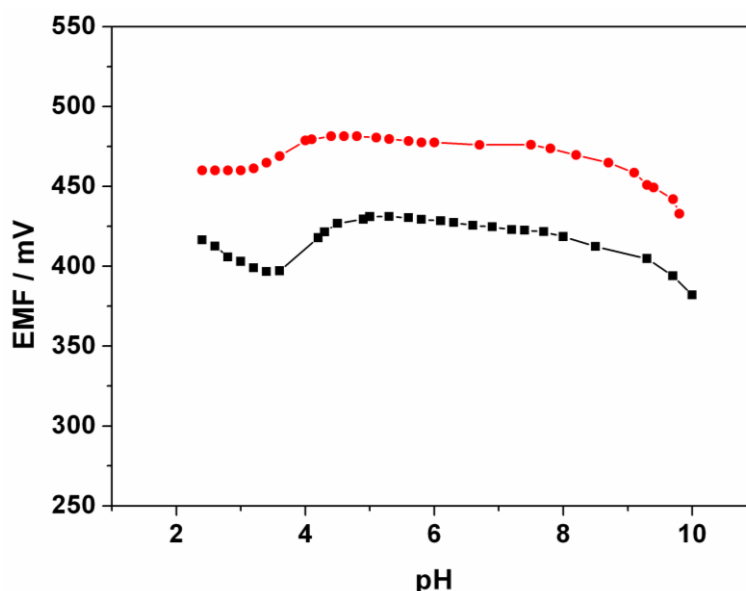
Figure 2. pH effect on the performance of Ag$^+$-ISE (Sensor No. **5b**). For ●: 1.0×10^{-2} M Ag$^+$, ■: 1.0×10^{-3} M Ag$^+$.

The resulting values of the selectivity coefficient are summarized in Table 3. The data show that the electrode based on thiaazacrown ether **5** exhibits a relatively high selectivity for Ag$^+$ over a large number of mono and bi-valent cations. As we all know, the selectivities and coordination abilities of crown ethers with transition metal ions depend on ring cavity size, ligand rigidity, the nature of

donor atoms and their disposition. From the results, we can conclude that the number of sulfur atom in the ring system instead of ring size and ligand rigidity play a key role on the potentiometric responses of the proposed Ag^+-ISEs. 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 [17, 18].

3.4. Effect of pH

The effect of pH on the electrode potential response was studied at two Ag^+ concentrations (1.0×10^{-2} and 1.0×10^{-3} M) where the pH was adjusted with HNO_3 or NaOH solutions and measured potentiometrically over the pH range from 2.3 to 10.0. The results shown in Fig. 2 indicate that a change of pH does not have an obvious effect on the electrode potential within pH range from 4.0 to 8.0. At the pH value below 4.0, high concentration of H^+ can go into the membrane to replace Na^+ and cause the drop of membrane potentiometry. The potential drop in the alkaline media could be consequence of AgOH precipitation [6]. Thus, appropriate potential measurement of Ag^+ was performed within pH 4.0-8.0.

4. CONCLUSIONS

A new Ag^+-ISE with N_3S_5-thiaazacrown ether as neutral carrier was successfully characterized. This Ag^+-ISE shows a low detection limit of 3.9×10^{-7} M Ag^+, a slope of 55.8 mV/decade, with a wide working range from 1.0×10^{-6} to 3.0×10^{-3} M Ag^+. The membrane plasticized with NPOE shows better potentiometric responses than DOS, DOP and DBP membrane. The electrode exhibits high selectivity and was easy to prepare and use.

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Supporting information:

Fig. S1. The mass spectrum of compound 4
Fig. S2. The ^{1}H NMR spectrum of compound 4
Fig. S3. The mass spectrum of compound 5
Fig. S4. The ^{1}H NMR spectrum of compound 5
Fig. S5. The ^{13}C NMR spectrum of compound 5
Fig. S6. The mass spectrum of compound 6
Fig. S7. The ^{1}H NMR spectrum of compound 7
Fig. S8. The ^{13}C NMR spectrum of compound 8

Fig. S1.

Fig. S2.
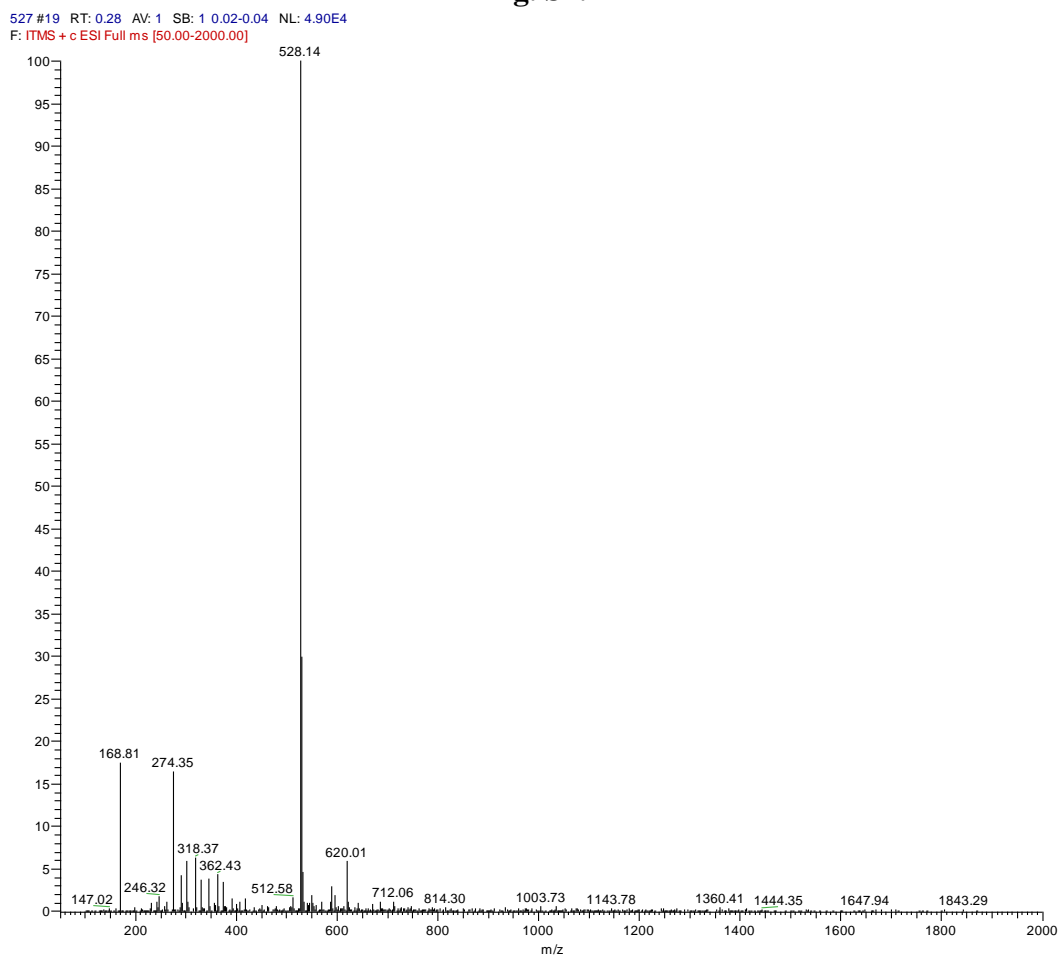

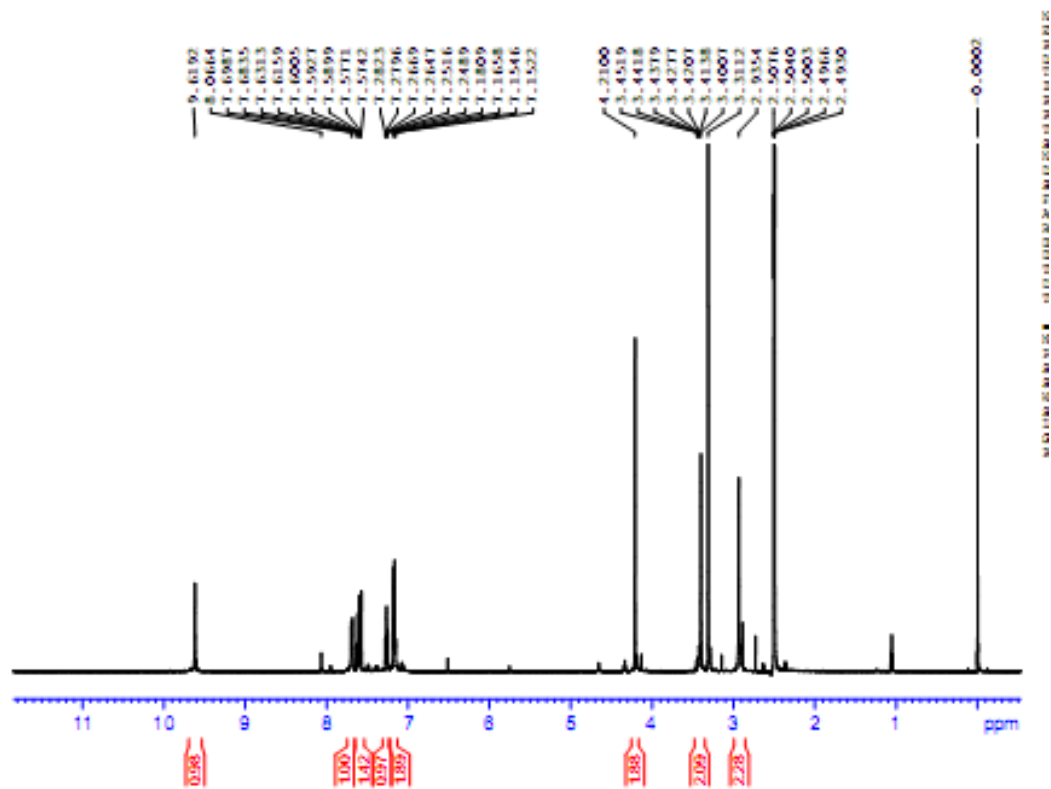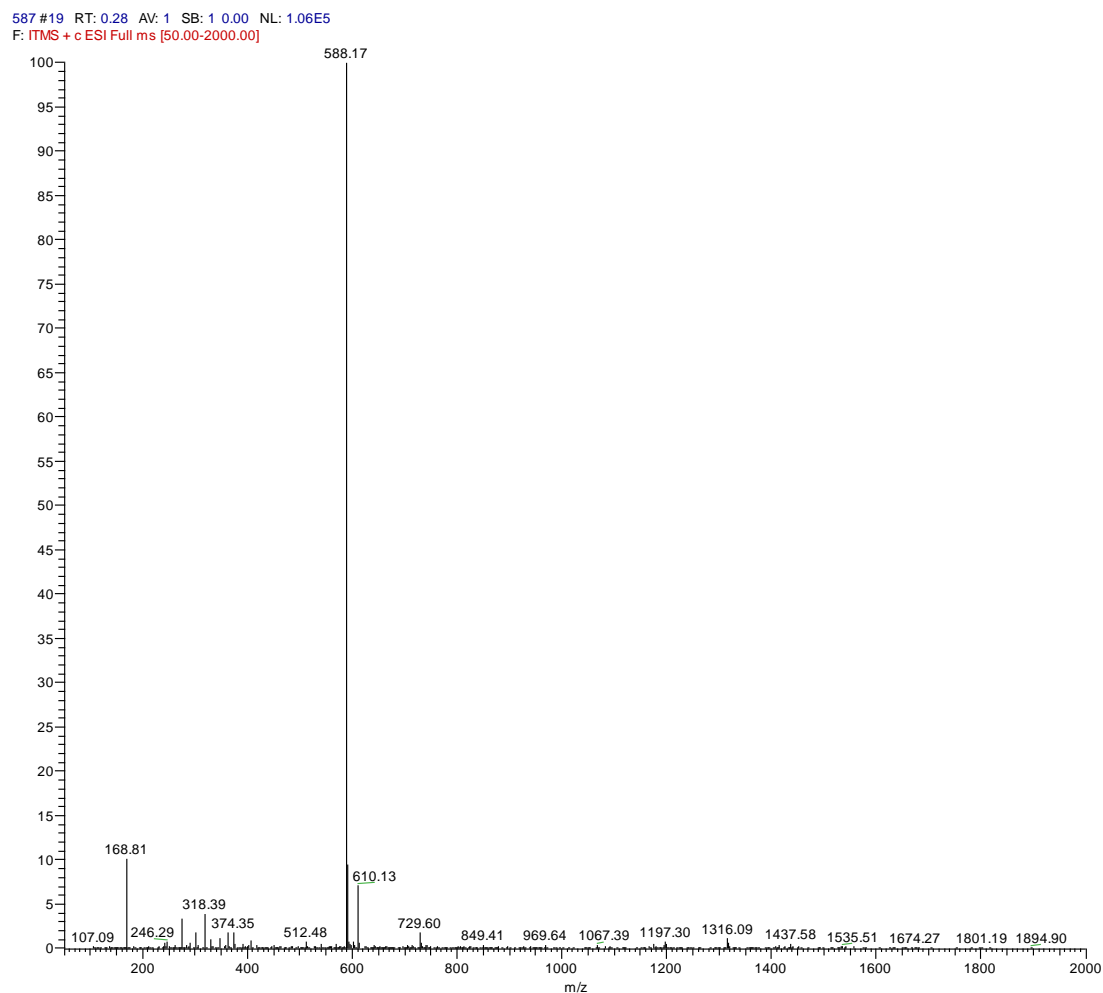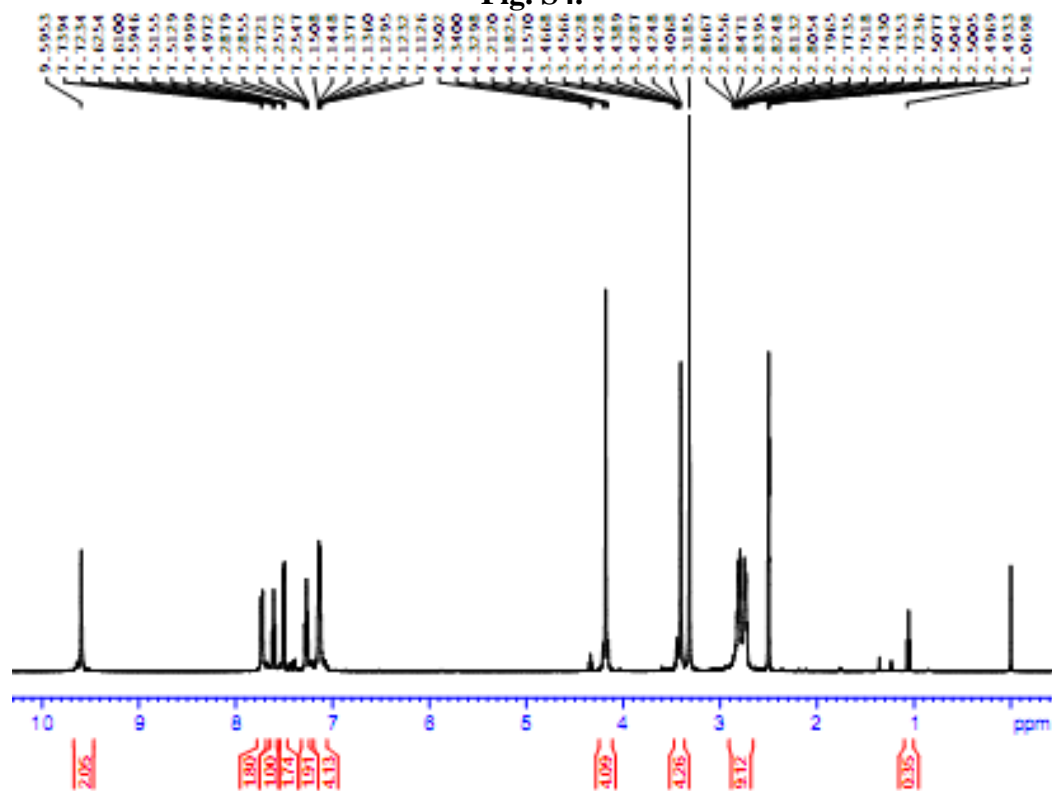**Fig. S3.**

Fig. S4.

Fig. S5.

Fig. S6.

Fig. S7.

Fig. S8.