

## Tetrahydrofuran-Containing Crown Ethers as Ionophores for NH<sub>4</sub><sup>+</sup>-Selective Electrodes

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The ammonium ion-selective electrodes (NH<sub>4</sub><sup>+</sup>-ISEs) based on the tetrahydrofuran(THF)-containing-16-crown-4 derivatives, 1,4,6,9,11,14,16,19-tetraoxocycloicosane (**L**<sup>1</sup>) and 5,10,15,20-tetramethyl-1,4,6,9,11,14,16,19-tetraoxocycloicosane (**L**<sup>2</sup>), were prepared and the electrode characteristics were tested. The conditioned NH<sub>4</sub><sup>+</sup>-ISEs (E1) based on **L**<sup>1</sup> with TEHP as a plasticising solvent mediator gave best results with near-Nernstian slope of 53.9 mV/decade of activity, detection limit of 10<sup>-1.9</sup> M, and enhanced selectivity coefficients for the NH<sub>4</sub><sup>+</sup> ion with respect to an interfering K<sup>+</sup> ion ( $\log K_{\text{NH}_4^+,\text{K}^+}^{\text{pot}} = -1.84$ ). This result was compared to other ammonium ionophores reported previously, for example, that of nonactin ( $\log K_{\text{NH}_4^+,\text{K}^+}^{\text{pot}} = -0.92$ ). The proposed electrode showed no significant potential changes in the range of 3.0 < pH < 9.0.

**Key Words** : Ammonium ionophore, Ion-selective PVC membrane electrodes, THF-containing crown ethers, Nonactin

### Introduction

From the clinical and environmental viewpoints, a convenient and exact determination of NH<sub>4</sub><sup>+</sup> ion in river water and urine samples is eagerly desired.<sup>1-5</sup> One of the most effective NH<sub>4</sub><sup>+</sup> ionophore is nonactin (Fig. 1), a natural antibiotic agent that is practically only employed ionophore in NH<sub>4</sub><sup>+</sup>-ISEs at present.<sup>6,7</sup> However, the selectivity of NH<sub>4</sub><sup>+</sup>-ISEs based on nonactin is poor for NH<sub>4</sub><sup>+</sup> relative to K<sup>+</sup> ( $\log K_{\text{NH}_4^+,\text{K}^+}^{\text{pot}} = -0.92$ ),<sup>8</sup> therefore, the NH<sub>4</sub><sup>+</sup> ion cannot be discriminated effectively from the K<sup>+</sup> ion. This limits its application to a low salt environment and produces the need for other treatments to avoid interference with K<sup>+</sup> ion.<sup>9-11</sup> Recently, some efforts to find suitable NH<sub>4</sub><sup>+</sup> ionophores were successful.<sup>12-18</sup> For examples, 20- to 21-membered crown ethers with bulky blocking subunits<sup>15,16</sup> and tripodal receptors with pyrazol end-groups<sup>17</sup> have been shown to be comparable or even superior to that of nonactin. But so far it is also true that there is no practically successful ionophore for NH<sub>4</sub><sup>+</sup> except nonactin till now.

On the other hand, we have reported that THF-containing

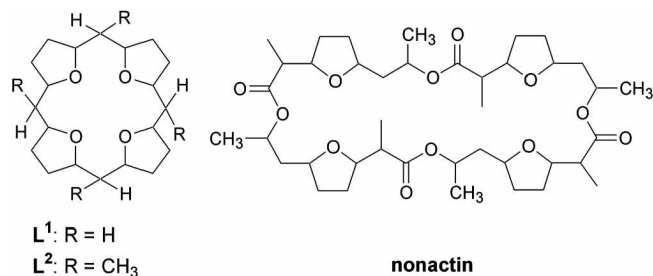
crown ethers with small substituents (R=CH<sub>3</sub>, R'=H) at four bridged *meso*-carbon position show excellent sensitivity and selectivity for Li<sup>+</sup> ion.<sup>19-21</sup> In the course of our consecutive works for the Li<sup>+</sup> ionophores, we realized that the analogue with methyl groups (R=R'=CH<sub>3</sub>) exhibited very high interference by NH<sub>4</sub><sup>+</sup> ion.<sup>19</sup> This result motivated us to require further examination and then we became interested in the THF-containing crown ethers in the view of the development of new candidates for NH<sub>4</sub><sup>+</sup> ionophores. In this standing point, we hypothesized that the bulkiness of *meso*-alkyl groups, which is related to the steric hindrance on complexation could be an important factor in an effective NH<sub>4</sub><sup>+</sup> ion sensing. Of course, there has been no attempt to measure the NH<sub>4</sub><sup>+</sup> responses by using the THF-containing-16-crown-4 derivatives.

The present ligands **L**<sup>1</sup> and **L**<sup>2</sup> (Fig. 1) were chosen by keeping this aspect in mind. Herein, we report the electrochemical characteristics of the NH<sub>4</sub><sup>+</sup>-ISEs based on these materials against the alkali and alkaline earth metal ions, and the effect of membrane composition and pH on the electrode responses.

### Experimental Section

**Chemicals.** Poly(vinyl chloride) (PVC, secondary standard) was product of Aldrich (Milwaukee), and tris(2-ethylhexyl) phosphate (TEHP), dioctyl phenylphosphonate (DOPP), and potassium tetrakis(*p*-chlorophenyl) borate (K1*p*CIPB, purum p.a.) were purchased from Fluka AG. The electrolyte solutions for the potentiometric measurements were prepared with doubly distilled water and chloride salts of high purity (Merck, pro analysis). THF was dried and purified by refluxing over sodium metal followed by distillation under N<sub>2</sub> atmosphere.

**Synthesis of THF-containing 16-Crown-4 Derivatives.** 1,1'-Methylenebis[5-(furfuryl) furan (**1**) and **L**<sup>2</sup> were prepared



**Figure 1.** Chemical structures of the THF-containing crown ether-type ammonium ionophores (**L**<sup>1</sup> and **L**<sup>2</sup>) and nonactin.

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**Table 1.** Composition of membranes and response characteristics as  $\text{NH}_4^+$ -ISEs

Electrode type	Membrane mass composition/wt%				Slope (mV/decade)	Detection limit (M)
	Ionophore	Matrix	Plasticizer	Additive*		
E1	$\text{L}^1$	PVC	TEHP	KTpCIPB 32.4	53.9	$10^{-5.0}$
	1.39	32.8	65.4			
E2	$\text{L}^1$	PVC	DOPP	KTpCIPB 32.4	50.8	$10^{-4.8}$
	1.58	32.8	65.1			
E3	$\text{L}^2$	PVC	TEHP	KTpCIPB 31.8	50.1	$10^{-4.8}$
	1.44	33.0	65.8			

\*mole % with respect to the ionophore.

according to the procedure reported previously.<sup>21</sup>

**1,4,6,9,11,14,16,19-tetraoxacycloicosa-1,3,6,8,11,13,16,18-octane (2):** To an ice-cooled mixture of 0.31 g (1.0 mmol) of **1**, 0.09 mL of dimethoxymethane and 100 mL of dichloromethane, 0.3 mL (2.4 mmol) of boron trifluoride-diethyl ether was added dropwise. The addition required 30 min and the reaction was continued for 2 days at room temperature, then extracted with diethyl ether, washed with 10%  $\text{NaHCO}_3$ , dried ( $\text{MgSO}_4$ ) and evaporated. The resulting solid was recrystallized from toluene twice to obtain **2** as white crystals in 6% yield.

**1,4,6,9,11,14,16,19-tetraoxacycloicosane ( $\text{L}^1$ ):** A mixture of 0.5 g of **2** and 200 mg of 10% Pd/C in 100 mL of tetrahydrofuran was pressured in a Parr reactor with hydrogen to 6 atm, and heated at 100 °C for 2 days. After removal of the catalyst by filtration and evaporation of solvent, the crude product was chromatographed using chloroform to obtain  $\text{L}^1$  as white crystals in 50% yield; mp 13–14 °C.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  3.60–4.08 (m, 8H), 1.81–2.05 (m, 8H), 1.19–1.79 (m, 16H). IR (KBr) 2995, 2950, 2890, 1420, 1330, 1084, 1025  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{20}\text{H}_{32}\text{O}_4$ : C, 71.39; H, 9.59; found: C, 70.57; H, 9.21.

**Preparation of Membranes and Electrodes.** The electrode membranes of PVC matrix type were fabricated by the method as reported earlier.<sup>23–25</sup> The membrane compositions were basically ~1.5 wt% of ionophore, ~33 wt% of PVC and ~65.5 wt% of plasticizer (TEHP and DOPP), and an adequate amount of KTpCIPB (~30 mol% with respect to the ionophore) was added as an anionic additive. Table 1 lists the composition of membranes (E1–E3) with ionophores and plasticizers. The membrane components were dissolved in freshly distilled THF which was then poured into a glass ring ( $d = 3.5$  cm) fixed on a glass plate. After standing for 24 h, a homogeneous PVC membrane of ~0.2 mm thickness was obtained. The prepared membrane was cut as circle with a diameter of 3.5 mm, which was mounted in lab-made Ag/AgCl electrode body or Philips IS-561 electrode body (Glasblaserei Moller, Zurich). After filling internal solution of 0.1 M  $\text{NH}_4\text{Cl}$ , the electrode was conditioned for 24 h by soaking in a 0.1 M  $\text{NH}_4\text{Cl}$  solution.

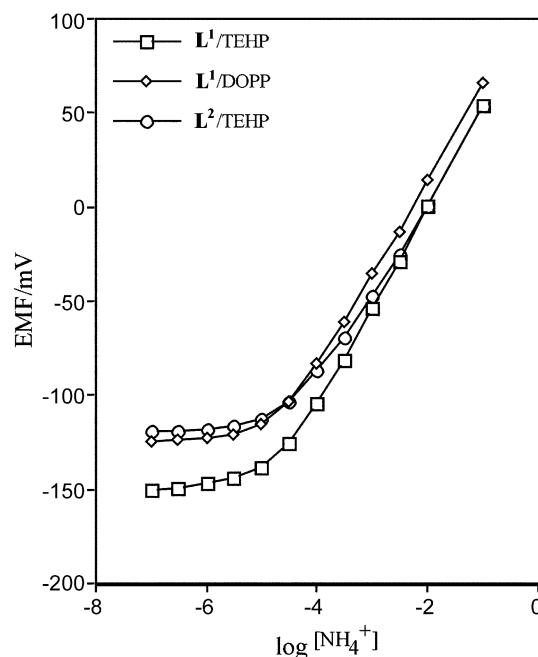
**Potential Measurements.** The electrochemical cell for the EMF measurements was as follows:

Ag; AgCl/3 M KCl/0.1 M  $\text{NH}_4\text{Cl}$ /sample solution/PVC membrane/0.1 M  $\text{NH}_4\text{Cl}$ /AgCl; Ag

EMF was measured relative to a Ag-AgCl double-junction reference electrode (Orion 90-02-00) using a digital pH/potentiometer (Orion 720A). All measurements were carried out at  $25.0 \pm 0.1$  °C. Potentiometric selectivity coefficients,  $K^{\text{pot}}_{\text{NH}_4^+, \text{M}}$  were determined by the separate solution method, which is one of the methods recommended by IUPAC,<sup>25</sup> on 0.1 M aqueous solutions of the chloride using the Nicolsky-Eisenman equation. The detection limits were also estimated according to the method suggested in IUPAC recommendation.<sup>25</sup>

## Results and Discussion

**Electrode Properties.** Figure 2 shows the calibration graphs of the electrodes E1–E3 (see Table 1) made from  $\text{L}^1$ ,  $\text{L}^2$ , TEHP, and DOPP together with constant amount of KTpCIPB and PVC. Calibration graphs were obtained by measuring known amount of ammonium chloride and plotting the concentrations against the corresponding EMF values obtained. The response characteristics of these electrodes are summarized in Table 1 with their com-



**Figure 2.** Potential responses of the THF-containing crown ethers-based  $\text{NH}_4^+$ -ISEs: ( $\square$ ) E1, ( $\diamond$ ) E2 and ( $\circ$ ) E3 in Table 1, respectively.

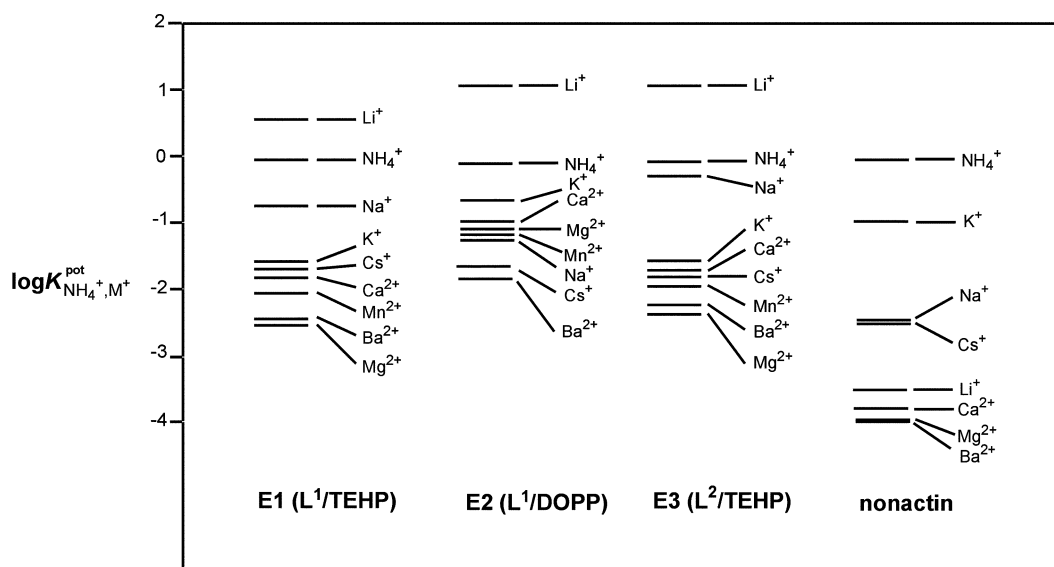


Figure 3. Selectivity coefficients,  $\log K^{\text{pot}}_{\text{NH}_4^+, \text{M}^+}$  for the NH<sub>4</sub><sup>+</sup>-ISEs based on L<sup>1</sup>-L<sup>2</sup> and nonactin for comparison.

positions. It was found that the potentiometric responses of E1 (L<sup>1</sup>) and E3 (L<sup>2</sup>) with TEHP and E2 (L<sup>1</sup>) with DOPP gave the response of 53.9, 50.1, and 50.8 mV/decade, respectively (Table 1 and Fig. 2). It is interesting that the electrodes made from L<sup>1</sup> (E1 and E2) show better response slopes, range of linearity, and detection limit than those of L<sup>2</sup> (E3). The higher sensitivity of L<sup>1</sup> on ammonium ion could be explained by the bulkiness of substituents, R on four bridged carbon position (L<sup>1</sup>; R=H, L<sup>2</sup>; R=CH<sub>3</sub>). The origin of ammonium sensing with many ionophores is known that the tetrahedral NH<sub>4</sub><sup>+</sup> tends to form H-bonds with negatively polarized ether oxygen atoms from the preorganized ionophores. The larger methyl group in L<sup>2</sup> may hinder, at least in part, the complexation of ammonium ion such that L<sup>1</sup> shows superior sensitivity than that of L<sup>2</sup>.

**Ion Selectivity.** The EMF values of the NH<sub>4</sub><sup>+</sup>-ISEs based on L<sup>1</sup> and L<sup>2</sup> for alkaline, alkaline earth metal, and Mn<sup>2+</sup> ions were measured, and the selectivity coefficients for the NH<sub>4</sub><sup>+</sup> ion with the respective interfering ion were calculated from separate solution method on 0.1 M solution of the chlorides at 25 °C. The resulting selectivity coefficients of the proposed electrodes are presented in Figure 3 with that of nonactin for comparison. As expected, both of L<sup>1</sup> and L<sup>2</sup> responded more selectively to NH<sub>4</sub><sup>+</sup> ion than to other ions except for Li<sup>+</sup> ion. The NH<sub>4</sub><sup>+</sup> is a univalent ion with an ionic diameter 2.96 Å,<sup>26</sup> which can be compared with that of K<sup>+</sup> ion (ionic diameter = 2.66 Å<sup>26</sup>). Therefore, as mentioned, the low NH<sub>4</sub><sup>+</sup>/K<sup>+</sup> selectivity for most crown ether type-based NH<sub>4</sub><sup>+</sup>-ISEs is due to the similar size of K<sup>+</sup> with NH<sub>4</sub><sup>+</sup> ion.<sup>27</sup> Once again, the E1 based on L<sup>1</sup> with TEHP afforded better selectivity than that of E2 or E3. Compared to nonactin ( $\log K^{\text{pot}}_{\text{NH}_4^+, \text{K}^+} = -0.92$ ),<sup>8,28</sup> the E1 based on L<sup>1</sup> showed higher NH<sub>4</sub><sup>+</sup> selectivity of about 70 times over K<sup>+</sup> ( $\log K^{\text{pot}}_{\text{NH}_4^+, \text{K}^+} = -1.84$ ), while suffering from increased interference of other ions including Na<sup>+</sup>. A similar selectivity of NH<sub>4</sub><sup>+</sup> over K<sup>+</sup> was also observed with L<sup>2</sup>. As a result, L<sup>1</sup> and L<sup>2</sup> with TEHP

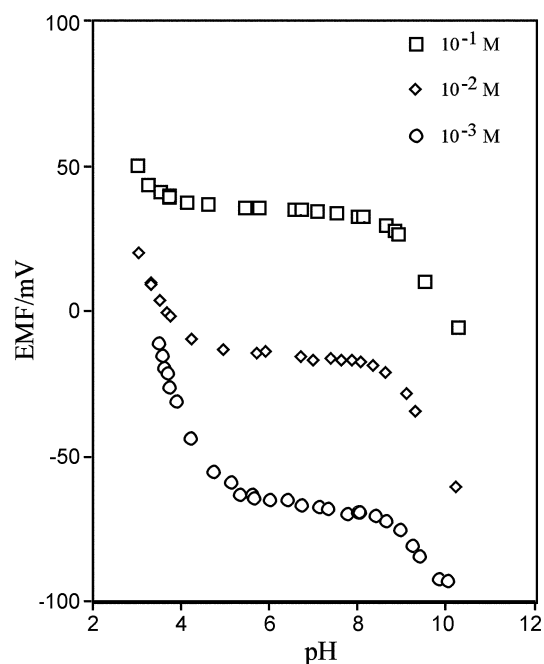


Figure 4. Effect of pH on the EMF response of the NH<sub>4</sub><sup>+</sup>-ISE (E1 in Table 1). HCl and NaOH were used to change the pH. (□)  $1.0 \times 10^{-1}$  M, (◇)  $1.0 \times 10^{-2}$  M and (○)  $1.0 \times 10^{-3}$  M.

suppress the response of K<sup>+</sup> ion more markedly than nonactin does.

As mentioned, NH<sub>4</sub><sup>+</sup> ion tends to form tetracoordinate complexes, while K<sup>+</sup> ion tends to preferably form hexacoordinate complexes. Thus, the higher NH<sub>4</sub><sup>+</sup>/K<sup>+</sup> selectivity can be explained that the THF-containing-16-crown-4 having basic four oxygen atoms in THF units are expected to form more stable complex with NH<sub>4</sub><sup>+</sup> than that formed with K<sup>+</sup>. The superior results for L<sup>1</sup> also suggest that the decrease of steric hindrance of L<sup>1</sup> by introducing four tetrahydrofuran oxygen could give a preferable geometry toward

$\text{NH}_4^-$  than those of  $\text{L}^2$  having methyl groups.<sup>29</sup> The most interference of  $\text{Li}^-$  ion for the THF-containing-16-crown-4-based  $\text{NH}_4^-$ -ISEs is due to the suitable ion size of lithium ion and geometric structure of the lithium-ionophore complex as previously reported.<sup>20,21,29</sup>

The pH-dependence of the electrode was studied for the pH range 2.5-10.0, adjusted by addition of hydrochloric acid and potassium hydroxide solutions having the same  $\text{NH}_4^+$  concentration as the test solution. The potentiometric responses of E1 to different concentrations of  $\text{NH}_4^+$  at above pH range are shown in Figure 4. E1 shows constant potentials between pH 3.0 and 9.0 in solutions which are  $10^{-1}$  M in  $\text{NH}_4^-$  solution. The response times for stable EMF readings were obtained within 30 s in wide range of concentration. Measurements were more stable with slow than with fast stirring. After lengthy storage, the electrode was reconditioned in 0.1 M  $\text{NH}_4^-$  solution for one day before using.

### Conclusion

We first report the  $\text{NH}_4^+$ -ISEs doped with the THF-containing crown ethers ( $\text{L}^1$  and  $\text{L}^2$ ) and considerable response and selectivity toward  $\text{NH}_4^+$  are observed. The electrode based on  $\text{L}^1$  with TEHP exhibited the best results in terms of sensitivity, detection limits, and selectivity for  $\text{NH}_4^-$  with respect to other metal ions. Especially, the proposed electrode afforded the higher  $\text{NH}_4^+/\text{K}^-$  selectivity compared with that of the electrode based on nonactin. The best performance of the  $\text{L}^1$ -based electrode can be understood that the bulky substituents on the bridged carbon of the ionophores seem to prevent complexation between  $\text{NH}_4^-$  and ionophores by a steric hindrance. The results represent the THF-containing crown ethers can be an alternative candidate for the  $\text{NH}_4^-$  ionophores. With further modification of the ionophore structure, additional enhancement for the selectivity toward  $\text{NH}_4^-$  ion would be possible.

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