

## Potentiometric Characteristics of Ion-Selective Electrodes Based on Upper-Rim Calix[4]crown Neutral Carrier

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Potentiometric characteristics of DOS plasticized PVC-based membranes containing upper-rim calix[4]crown neutral carrier to various metal cations and protonated alkylamines have been examined. Although the calix[4]crown-based membrane electrodes exhibited substantial emf responses to alkali and alkaline earth metal cations, their high detection limits ( $-\log[\text{Cs}^+] = 4.5$ ) and sub-Nernstian response slopes ( $48 \text{ mV/pCs}^+$ ) to the most selective cation, cesium, indicate that the metal cation complexing ability of calix[4]crown is much weaker than that of macrocyclic crown ethers. However, the calix[4]crown-based membrane electrodes exhibited near-Nernstian response slopes ( $56 \text{ mV/decade}$  for  $\text{hexylNH}_3^+$ ) with low detection limits ( $\log[\text{hexylNH}_3^+] = -6.7$ ) to most alkylammonium ions compared to those of blank (DOS plasticized PVC membrane with no ionophore) or crown ether-based membranes. While the selectivity patterns of blank and crown ether-based membranes are determined primarily by the lipophilicity of alkylammonium ions, the membranes doped with calix[4]crown ionophore could effectively discriminate the steric shapes of nonpolar alkyl groups of alkylammonium ions.

### Introduction

Ion-selective electrodes (ISEs), especially those with neutral carrier-based solvent polymeric membranes, have been studied for more than three decades. ISEs are now routinely employed for direct potentiometric measurements of various ionic species in environmental, industrial and clinical samples.<sup>1,2</sup> And yet, even in the nineties a few hundreds articles related to ISEs are published every year. While many recent articles deal with the technological advances, *i.e.*, microfabrication and integration of miniaturized potentiometric probes,<sup>3</sup> and application of such sensors for point-of-care or *in vivo* clinical analysis,<sup>4</sup> fundamental studies such as design, synthesis and potentiometric characterization of new ionophores that are either more selective than those previously reported or capable of recognizing additional ionic species still remain as the main topics in ISE researches.<sup>5,6</sup>

Myriad of cyclic and acyclic ionophores with well defined coordination sites formed by oxygen, nitrogen or sulfur have been synthesized and examined for such purposes. In recent years, a new series of compounds known as calixarenes, cyclic oligomers of phenol-formaldehyde condensates, has emerged as promising synthetic ionophores;<sup>7-14</sup> 4 to 8 phenolic units in calixarene compounds provide highly stable molecular platform on which are numerous type of preorganized functional groups capable of ion and/or molecule reception.

For example, several groups have reported that PVC-based membranes with calix[4]arenes derived with symmetric or asymmetric ester chains at the lower-rim exhibit excellent selectivity to alkali metal ions, especially to sodium;<sup>15-21</sup> those with 6 membered crown ethers are selective to cesium;<sup>22</sup> those with ligating functional groups containing soft donor atoms, such as nitrogen and sulfur, sensitively respond to the activity changes of heavy metal ions (*e.g.*,  $\text{Pb}^{2+}$ ,  $\text{Ag}^+$ ).<sup>13,14,23-25</sup> Odashima *et al.*<sup>26</sup> and Chan *et al.*<sup>27</sup> examined

the potentiometric responses of calix[6]arene esters to various protonated amines; they postulated that protonated primary amines form tripodally hydrogen bonded complex with the inward-directed ester carbonyl groups of calixarene derivatives.

Recently, Paek and Ihm<sup>28,29</sup> examined molecular recognition properties of upper-rim calix[4]crowns (compound I in Figure 1) by extraction experiment of solid alkali metal or ammonium picrates into chloroform solution of the host; it was observed that they exhibit high extraction efficiencies for protonated primary amines compared with those for ammonium or alkali metal cations. Based on the CPK (Corey-Pauling-Kortum) molecular modeling study and simple molecular mechanics calculation, they suggested that am-

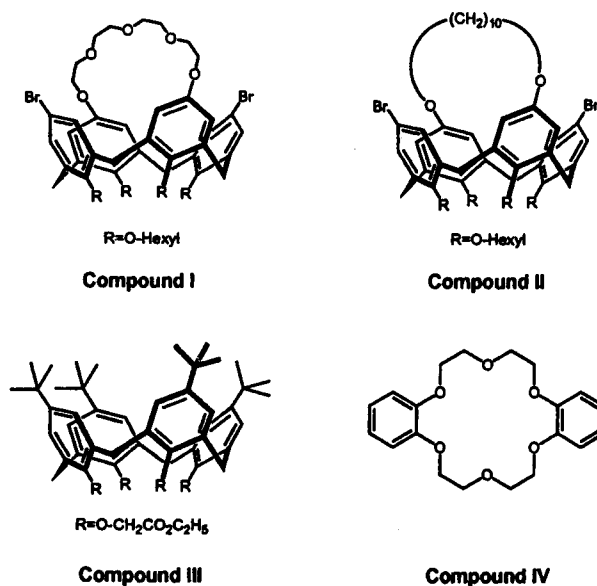


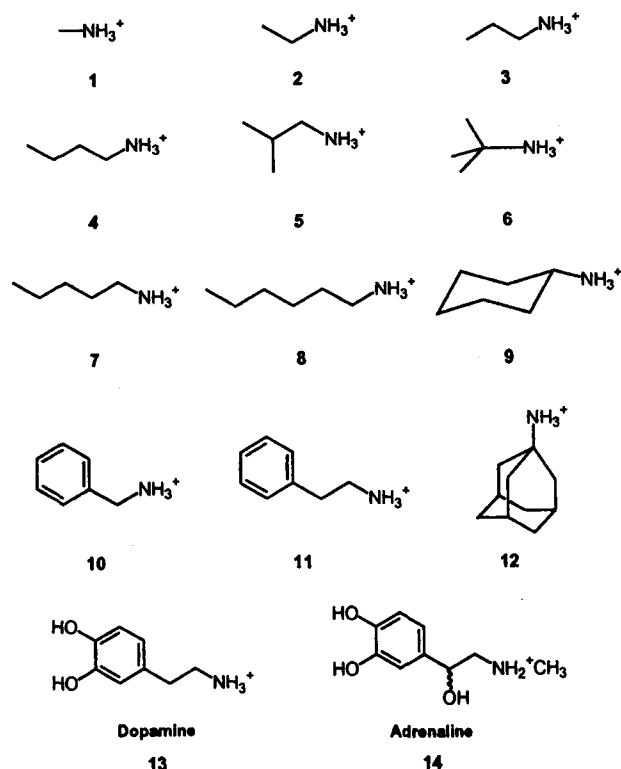
Figure 1. Structure of ionophores.

monium or alkali metal ions are bound only to partially organized oligoether moiety, while protonated primary amine could be bound to both hydrophobic cavity and hydrophilic oligoether unit of the host simultaneously. We may exploit such high extraction efficiencies of upper-rim calix[4]crown for protonated primary amines to develop amine-selective ISEs. The comparison of molecular recognition properties of various ionophores that contain similar coordination sites in their structures may also provide us with valuable insights on designing new type of ionophores for organic ions. In this contribution, we report the potentiometric response characteristics of PVC-based ISE membranes prepared with calix[4]crown as well as three different ionophores shown in Figure 1 to alkali and alkaline earth metal ions, and to various protonated amines.

## Experimental

**Reagent.** Poly(vinyl chloride) (PVC) and bis(2-ethylhexyl) sebacate (DOS) were purchased from Fluka Chemie AG (Buch, Switzerland). Dibenzo-18-crown-6 (DB 18C6) and 4-tert-butylcalix[4]arene-*o,o',o'',o'''*-tetraacetic acid tetraethyl ester (compound III) were the products from Aldrich (Milwaukee, Wisconsin). Two other calix[4]arene derivatives, compounds I and II, were synthesized according to the method described in reference.<sup>28,29</sup> Alkylamines and their HCl salt shown in Figure 2 were obtained from Sigma Chemical Co. (St. Louis, MO, USA). All other chemicals used were analytical-reagent grade. Standard solutions and buffers were prepared with deionized water.

**Preparation of electrodes and their potentiometric evaluations.** The PVC-based membranes were



**Figure 2.** Structure of organic ammoniums examined in this study

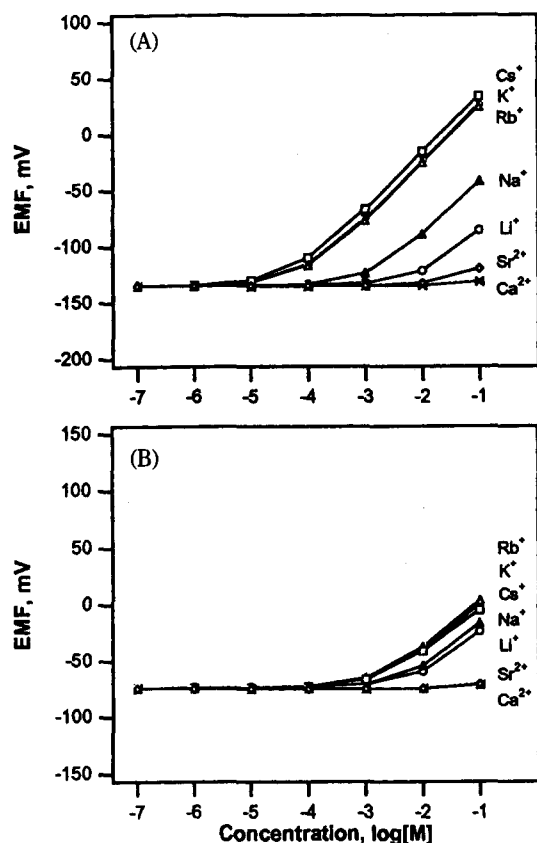
prepared with 1.2 wt% ionophore, 33 wt% PVC and 65.8 wt% DOS. These membrane components dissolved in 1 mL THF were then poured into a glass ring (i.d. 18 mm) placed on a slide glass, and dried overnight at room temperature. Small disks were stamped out from the cast films and mounted in Philips electrode bodies (IS-561; Glasblaserei Mler, Zich, Switzerland). 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 dynamic response curves were obtained by adding standard solutions to 200 mL of magnetically stirred background electrolyte (0.05 M Tris-HCl, pH 7.2) every 100 s to vary the concentrations of primary ions (alkali, alkaline earth metal and protonated alkyl amine ions) stepwise from  $10^{-6}$  to  $10^{-1}$  M, and the measurements of emf values were taken every second at room temperature. Selectivity coefficients were estimated according to the separate solution-matched potential method (IUPAC SSM II method).<sup>30</sup>

## Results and Discussion

To compare the cation recognition properties of calix-arene derivatives, *i.e.*, compound I and II, with DB18C6 in a DOS-plasticized PVC medium, their emf responses to ammonium, alkali and alkaline earth metal ions have been examined first. The results obtained with compound I and II are shown in Figure 3, and that with DB18C6 is presented elsewhere.<sup>31</sup>

Examining the structure of compound I, we may presume that it has two possible cation binding sites, *i.e.*, the upper-rim oligoether unit and the lower-rim alkoxy groups. However, since the emf response for the membranes based on compound II, in which the  $-O-(CH_2)_{10}-O-$  chain instead of oligoether moiety bridges the two alternate phenyls of calix[4]arene, to metal ions are virtually the same as those of PVC/DOS membranes with no ionophores (compare Figure 3 (A) and (B)), we may conclude that the lower-rim alkoxy groups play negligible role in cation recognition. Thus, metal cations diffused into the membrane are expected to form complexes primarily with the upper-rim oligoether unit of calix[4]crown. However, the sub-Nernstian slope (48 mV/pCs<sup>+</sup>) and high detection limit ( $-\log[C_s^+] = 4.5$ ) of compound I-based electrode indicate that the upper-rim calix[4]crown is a less effective ligand for metal cations than cyclic crown ethers, such as DB18C6. Paek and Ihm also reported that compound I has poor extractability for ammonium and alkali metal cations (<5%).

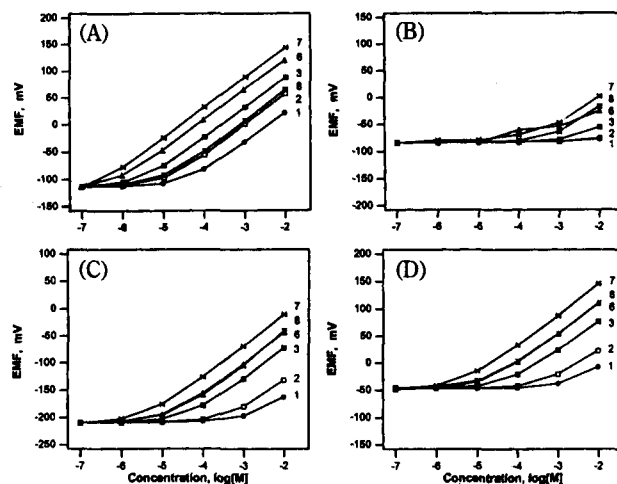
Cation recognition properties of the upper-rim calix[4]crown have been examined further by comparing the potentiometric responses of membrane electrodes based on compound I, III and DB18C6 to various alkylammonium ions. Figure 4 displays the potentiometric responses of those three electrodes, including that of a blank membrane electrode, to simple primary alkylammonium ions. Since the calix[4]crown-based electrode exhibits negligible response to proton activity at pH>6.0, and alkylamines ( $pK_a = 9.5-11$ )



**Figure 3.** Potential responses of PVC/DOS membrane electrodes based on compound I(A) and II (B) to alkali and alkaline earth metal cations.

are mostly in their monocationic forms by protonation at near neutral pH, the response behavior of all electrodes to amine derivatives was examined at pH 7.2 (0.05 M Tris-HCl buffer).

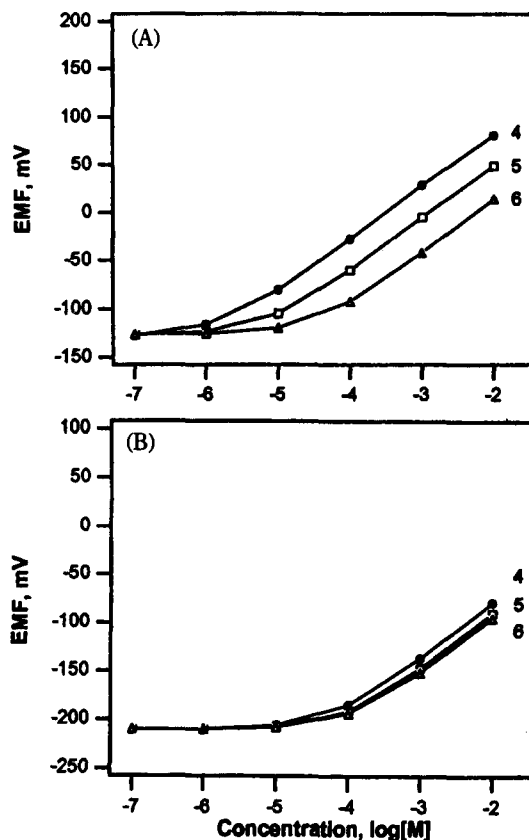
Protonated amines may approach the binding site of calix[4]crown in two directions: through the lower-rim channel of four -O-hexyl groups and the cavity of phenolic ring, and/or directly to upper-rim oligoether unit. In either case, the formation of alkylammonium-calix[4]crown complex is expected to be dependent on the steric bulkiness around the  $-\text{NH}_3^+$  group. Another factor of consideration is the distribution coefficients of alkylamines to organic membrane phase, which typically reflect the sequence of their lipophilicity. Figure 4(D), the emf responses of the blank PVC/DOS-based membrane, exemplify such a sequence:  $8 > 9 \approx 7 > 4 > 3 > 2 > 1$  alkylammonium ions shown in Figure 2. Addition of DB18C6 to PVC/DOS-based membrane, although it increased the total emf responses of the electrode to alkylammonium ions, did not change this sequence. On the other hand, Figure 4(A) shows that the calix[4]crown-based membrane electrode can discriminate the ammoniums with bulky alkyl groups and the order of its selectivity becomes;  $8 > 7 > 4 > 9 \approx 3 \approx 2 > 1$ . Figure 5 clearly demonstrates the steric shape recognition ability of calix[4]crown: while both blank and DB18C6-doped membranes exhibit similar selectivities to *n*-butyl (4), *sec*-butyl (5) and *tert*-butyl ammoniums (6), the calix[4]crown-doped membranes differentiates them in the order of the bulkiness of alkyl group,



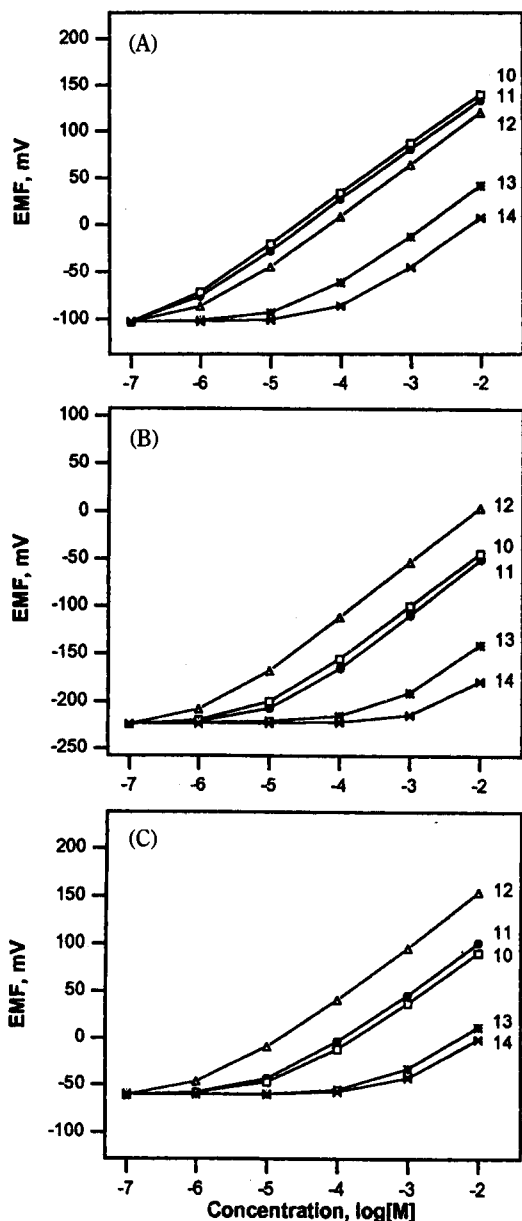
**Figure 4.** Potential responses of electrodes based on compound I (A), III (B), IV (C), and blank PVC/DOS membrane (D) to simple primary amines at pH 7.4 (Tris-HCl buffer). Numbers on each calibration curve correspond to the alkylammonium ions shown in Figure 2.

*i.e.*,  $4 > 5 > 6$ .

Calix[6]arene esters are known to respond selectively to alkylammonium ions as the  $-\text{NH}_3^+$  group forms tripodal hydrogen bonding with the lower-rim ester functional groups.<sup>21,22</sup> However, the calix[4]arene ester derivative (compound III)-



**Figure 5.** Potential responses of electrodes based on compounds I (A) and IV (B) to *n*-, *sec*- and *tert*-butylammonium (4, 5, and 6 in Figure 2) at pH 7.4.



**Figure 6.** Potential responses of electrodes based on compound I (A), IV (B), and blank PVC/DOS membrane (C) to adamantan-ammonium (12) and protonated amines with phenyl derivative substituents (10, 11, 13 and 14).

based membrane electrode gave rise to inferior emf responses to all alkylammonium ions compared to those of the blank membrane-based electrode. This result indicates that alkylammonium ions may not easily enter through the lower-rim channel of calix[4]arene derivatives. The response behavior of

compound II-based membrane electrode to alkylammonium ions was similar to that of the blank membrane-based electrode. These evidences may suggest that the  $-\text{NH}_3^+$  group of alkylammonium ions do not form hydrogen bonded complexes with the -o-hexyl group of compound II.

Finally, we examined the response behavior of calix[4] crown-based membrane electrode to adamantanamine (12) and four other amine derivatives with phenyl substituents (10, 11, 13, and 14). These results are summarized in Figure 6 and Table 1. Comparison of emf responses shown in Figures 6(A) and 6(B) demonstrates again that calix[4] crown-based membrane electrode is capable of discriminating the steric shape of amine derivatives; its total emf response to adamantan ammonium (215 mV from 0 to  $10^{-2}$  M in a 0.05 M Tris-HCl buffer) remained virtually the same as that of the blank membrane-based electrode (223 mV under the same condition). It indicates that the emf response of calix[4]crown-based electrode to alkylammonium ions with bulky substituents results from their large distribution constants, but not from the host-guest complexation. The total emf responses of calix[4]crown-based electrode to benzyl and 2-phenylethyl-ammonium (10 and 11) were notably increased from those of the blank membrane-based electrode (ca. +80 mV), indicating the formation of a stable host-guest complex within the membrane phase. The increase in its total response to protonated dopamine (13), ca. +73 mV (in the  $0\text{--}10^{-2}$  M range), was also about the same magnitude as that to the other two phenylamine derivatives. Although the dopamine selectivity of calix[4]crown-based electrode over potassium ( $\log K_{13,K}^{\text{POT}} = -0.6$ ) was improved compare to that of the calix[6]arene ester-based electrode ( $\log K_{13,K}^{\text{POT}} = 0.5$ ),<sup>25</sup> its high detection limit ( $2.8 \times 10^{-6}$  M) and low response slope (36.5 mV/decade) for dopamine still limit its practical utility. Nevertheless, this result suggests that catecholamine-selective ionophores with reduced selectivity toward alkali and alkaline earth metal cations may be designed modifying the upper-rim calix [n]crown compounds.

## Conclusion

Potentiometric characteristics of DOS plasticized PVC-based membranes containing upper-rim calix[4]crown neutral carrier with four lower-rim -OR (R=hexyl) groups (compound I) to various metal cations and protonated alkylamines have been examined. Comparing the emf responses of the membranes containing compound I with those containing compound II, which has decyl bridge in substitute for oligoether linkage at the upper-rim, it was found that the upper-rim crown is the prime cation recognition site of compound I. However, as indicated by the high detection limits ( $-\log[\text{Cs}^+] = 4.5$ ) and sub-Nernstian

**Table 1.** Organic ammonium selectivities of PVC/DOS membrane electrodes containing calix[4]arene derivatives

Ionophore	Slope <sup>a</sup>	Detection limit <sup>b</sup>	Selectivity coefficient ( $\log K_{s,j}^{\text{POT}}$ )													
			1	2	3	4	5	6	7	8	9	10	11	12	13	14
Blank	53.8	5.9	-3.3	-2.4	-1.8	-1.2	-1.5	-1.6	-0.7	0	-0.6	-0.7	-0.6	0.2	-2.6	-3.0
Compound I	55.7	6.7	-2.4	-1.9	-1.7	-1.2	-1.9	-2.7	-0.7	0	-1.3	-0.6	-0.5	-1.0	-2.4	-3.0
Compound IV	55.2	6.0	-3.4	-2.6	-2.1	-1.5	-1.8	-1.9	-0.7	0	-0.5	-0.6	-0.7	0	-2.6	-4.0

<sup>a</sup>Response slopes in mv/decade with respect to  $[\text{hexylNH}_3^+]$  (range:  $10^{-5}\text{--}10^{-2}$  M), <sup>b</sup> $-\log[\text{hexylNH}_3^+]$ .

response slopes (48 mV/pCs<sup>+</sup>) of compound I-based membranes, calix[4]crown is a less selective ionophore for metal cations than macrocyclic crowns. On the other hand, calix[4]crown-based membrane exhibited substantially increased emf responses to most alkylammonium ions compared to those of blank or crown ether-based membranes. Although the potentiometric selectivities of the electrode were determined primarily by the lipophilicity of alkylammonium ions, it was seen that the calix[4]crown ionophore could discriminate the steric shapes of nonpolar alkyl groups.

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