

On the Selection of the Optimal Plasticizer for Calix[*n*]arene-Based Ion-Selective Electrodes: Possible Correlation between the Ion Selectivity and the ‘Softness’ of the Plasticizer

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Abstract. A criterion for the selection of a suitable plasticizer for calix[*n*]arene-based ion-selective electrodes is discussed. The cation selectivity of plasticized membranes without the ligand was first measured as a reference. The membranes can be roughly classified into two groups. The first group shows cation selectivity in the order $\text{Cs}^+ < \text{Rb}^+ > \text{K}^+ > \text{Na}^+ > \text{Li}^+$. The membranes in the second group are made of phosphorus plasticizers, which show a selectivity in the reverse order. The plasticizers in the first group featured a linear relationship between the dipole moment of the plasticizer (calculated by a PM3 method) and the ratio of cesium selectivity to lithium selectivity. The linear relationship supports the view that the polar membrane which includes a ‘soft’ plasticizer with a large dipole moment shows selectivity for Cs^+ , whereas the nonpolar membrane including the ‘soft’ plasticizer with the small dipole moment shows much lower selectivity for Cs^+ . Next, 2-fluorophenyl-2’-nitrophenyl ether (FPNPE) which showed the highest Cs^+ selectivity and tris(2-ethylhexyl)phosphate (TEHP) which showed the highest Li^+ selectivity were mixed in an appropriate ratio to make membranes with a different affinity for ‘hard’ ions. The metal selectivities of several crown-based and calixarene-based ionophores were examined in these membranes. Although a few exceptions exist, the polar ‘soft’ membrane is favorable when the interfering metal ion is ‘hard’, whereas the ‘hard’ membrane is favorable when the interfering metal ion is ‘soft’.

Key words: Calixarenes, ion-selective electrodes, plasticizer.

1. Introduction

Numerous ligands have been synthesized and examined as neutral carriers for ion selective electrodes because it was commonly believed that molecular design of the neutral carrier directly reflects their selectivity. In order to achieve an excellent sensor system, a neutral carrier should possess at least the following four properties: selectivity, lipophilicity, mobility, and complex formation constant [1]. However, we found that a tetraethyl ester derivative of *p*-*tert*-octylcalix[4]arene possessed excellent Na^+ selectivity [2], even though there is no difference in the ionophoric

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cavity component compared to *p-tert*-butylcalix[4]arene tetraethyl ester which was previously reported by McKervey *et al.* [3]. A similar report has been published by Shono *et al.* [4], who found that a decrease in the selectivity is observed when a debutylated calix[4]arene was used as a ligand.

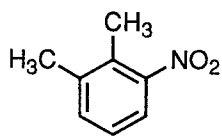
It may be inferred from the foregoing findings that the design of the ionophoric cavity is not the sole factor which governs the selectivity of ligands for ion-selective electrodes. So far, many trials directed toward substitution with long alkyl chains have been made in order to decrease hydrophilicity of the ligand. In such cases, however, it is very interesting to note that the selectivity, but not the lifetime, is improved. One can state that a method for improving the selectivity consists not only in the design around the ionophoric cavity but also in the conditioning of the environment. There are two possible factors which condition the environment around the ligand: one is poly(vinyl chloride) (PVC) and another is plasticizer. Armstrong *et al.* reported that a difference in the dielectric constant of the PVC membrane is induced by an initiator segment [5]. Pungor *et al.*, using impedance measurements, also reported that a decrease in the dielectric constant of the membrane is observed in the presence of PVC [6]. However, an effect of the plasticizer is also significant because it is a major component in the membrane and has an important role as the membrane solvent which interacts directly with the ligand. Fiedler investigated effects of plasticizers on both potassium and calcium selective electrodes [7]. He concluded that a plasticizer with a low dielectric constant is suitable for the potassium ion-selective electrode based on valinomycin, whereas a high dielectric constant is needed for the divalent cation-selective electrode. On the other hand, Shono *et al.* reported that 2-nitrophenyl octyl ether, which has a relatively high dielectric constant, is a more suitable plasticizer for both sodium and potassium electrodes based on crown ethers [8]. These results consistently demonstrate the importance of plasticizers, but predicting the optimum plasticizer is still difficult.

In this paper, we report an investigation into the characterization of these plasticizers in relation to an attempt to predict suitable plasticizers for several calix[4]arene-based ion-selective electrodes.

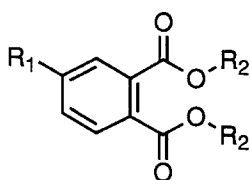
2. Experimental

2.1. PREPARATION OF ION-SELECTIVE ELECTRODES AND MEASUREMENTS OF MEMBRANE POTENTIALS

The preparation of ion-selective electrodes and the measurement of membrane potentials have been described previously [2]. Chloride ion was used as a counter anion of alkali and alkaline earth metals, nitrate ion was used for the other cations, without buffering. First, sodium selectivity without ligand was measured for all



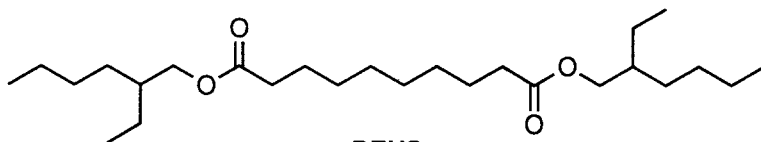
2,3-DMNB



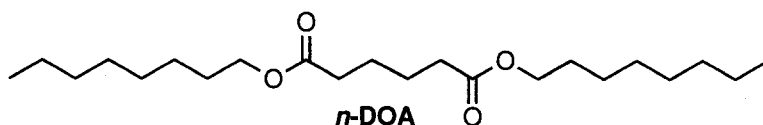
DEHP: R₁=H, R₂=2-ethylhexyl

NO₂-DEHP: R₁=NO₂, R₂=2-ethylhexyl

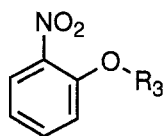
NO₂-DOP: R₁=NO₂, R₂=*n*-octyl



DEHS



***n*-DOA**



NPPE: R₃=phenyl

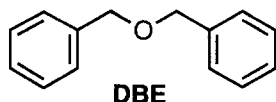
FPNPE: R₃=2-fluorophenyl

NPOE: R₃=*n*-octyl

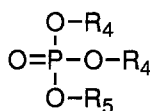
NPNE: R₃=*n*-nonyl

NPDE: R₃=*n*-decyl

NPDDE: R₃=*n*-dodecyl



DBE

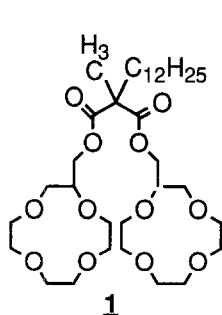


TEHP: R₄=R₅=2-ethylhexyl

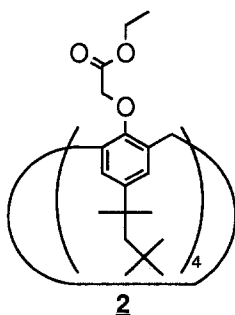
TCP: R₄=R₅=cresyl

DOPP: R₄=octyl, R₅=phenyl

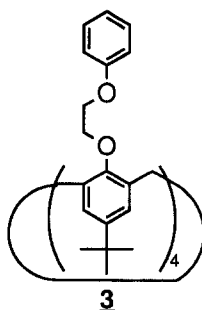
Plasticizers used in this report



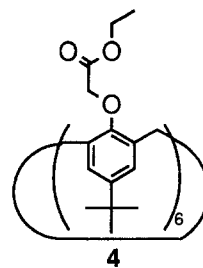
1



2



3



4

Ligands used in this report

plasticizers. The determination of selectivity coefficients was performed by the separate solution method (SSM) at 25 °C. The pH dependence of all the ligands in FPNPE was checked, and all the ligands were non-responsive to hydrogen ion in the region of pH 4–9. Selectivity coefficients were calculated by the Nicolsky–Eisenman equation from the data at 10^{-1} mol dm $^{-3}$ except for mercury (10^{-2} mol dm $^{-3}$ at pH 2.2).

2.2. CALCULATION OF DIPOLE MOMENTS

Dipole moment of the plasticizers was calculated with a semiempirical molecular orbital method (MNDO-PM3) [9]. The input structures of these compounds were established by the combination of the standard bond lengths found in the crystal structures [10]. Molecular structures were optimized with the program MOPAC Ver. 6 [11] using the PM3 Hamiltonian, and dipole moments were calculated on the basis of the structures obtained. These calculations were performed on the engineering workstation system: SUN 4/10 and IRIS4D35G.

3. Results and Discussion

Figure 1 shows selectivity profiles of numerous plasticizers in the absence of the ligand. A decrease in sodium selectivity against divalent cations was observed in nitrophenyl derivatives, which possessed the highest dipole moment. This result coincides with that obtained by Fiedler [7]. Interestingly, these plasticizers can be classified into two categories by the order of ion selectivity. One is a group of phosphorus derivatives which show an order of $\text{Li}^+ > \text{Na}^+ > \text{K}^+ > \text{Rb}^+ > \text{Cs}^+$, whereas the other plasticizers show a reverse order; $\text{Cs}^+ > \text{Rb}^+ > \text{K}^+ > \text{Na}^+ > \text{Li}^+$, except for DBE. DBE showed high specificity towards silver ion and the selectivity order is $\text{Cs}^+ > \text{Rb}^+ > \text{K}^+ > \text{Li}^+ > \text{Na}^+$. We found that there is a linear relationship between potentiometric cesium/lithium selectivity ($\log K_{\text{Cs}^+,\text{Li}^+}^{\text{pot}}$) and the dipole moment of the plasticizer calculated by a PM3 method, except for phosphorus ones (Figure 2). Only DBE deviates from the linear relationship in Figure 2. As DBE is useful as an ammonium selective ligand, DBE may play a specific role as a neutral carrier. On the other hand, phosphorus plasticizers such as TEHP do not satisfy this linearity because they generally show high lithium selectivity. This implies a minus value on the x axis, regardless of the plus value for the dipole moment.

Ion concentration vs. potential curves of two plasticizers, FPNPE and TEHP, are shown in Figures 3 and 4, respectively. As it is clearly shown in Figure 3, the sensitivity to cesium ion in the case of FPNPE (55 mV/decade in the region between 10^{-3} to 10^{-4} , see Table I) is much higher than that in the case of TEHP (44 mV/decade). On the other hand, the sensitivity to lithium ion (22 mV/decade in the region between 10^{-3} to 10^{-4}) in the case of FPNPE is much lower than that in the case of TEHP (63 mV). This indicates the fact that the membrane based on FPNPE has a great affinity for ‘soft’ cations such as cesium, and the membrane

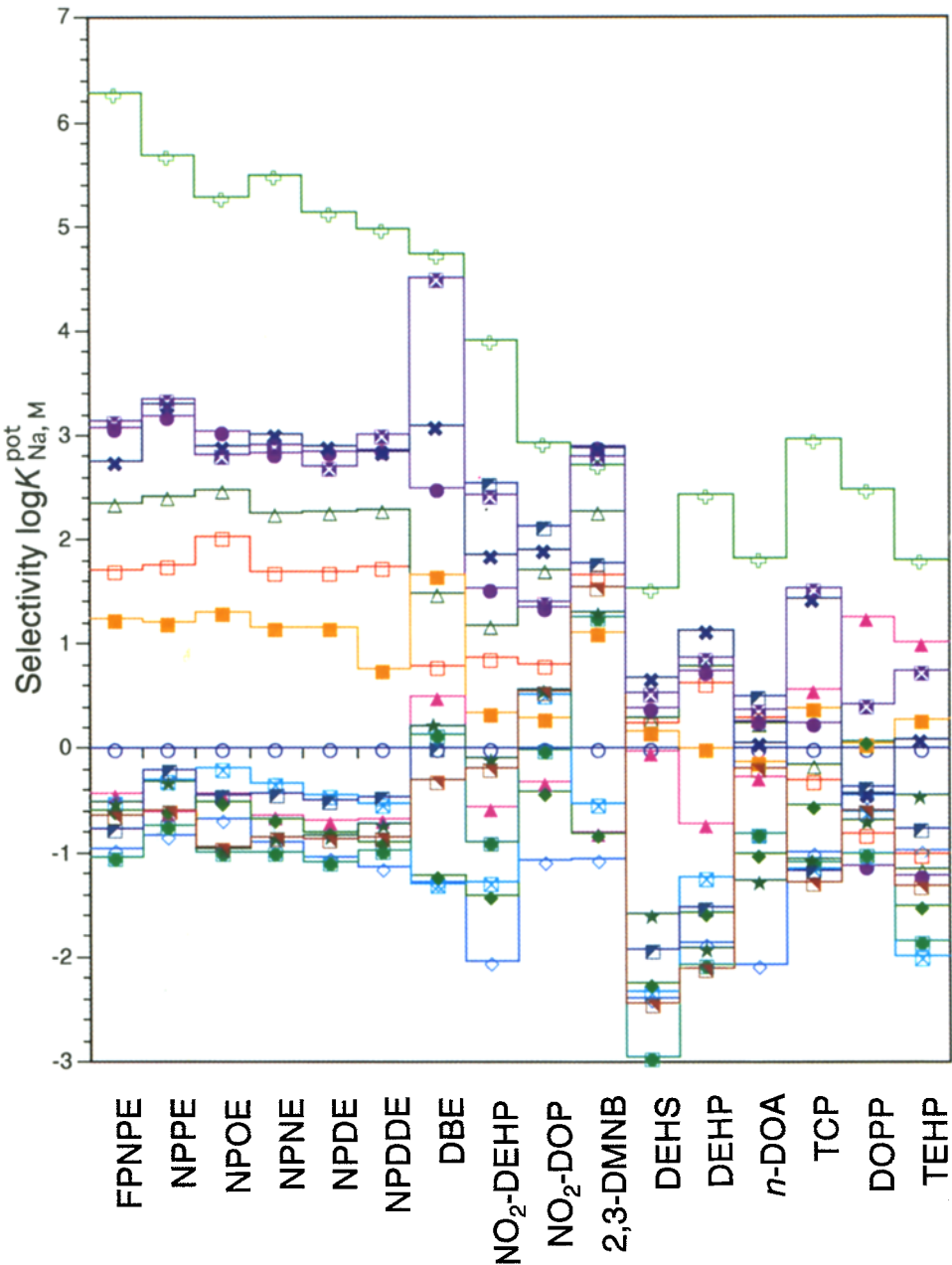


Fig. 1 Selectivity profiles of numerous plasticizers; -○- Na^+ ; -□- K^+ ; -△- Rb^+ ; -●- Cs^+ ; -■- NH_4^+ ; -▲- Li^+ ; -◇- Mg^{2+} ; -◆- Ca^{2+} ; -⊠- Ba^{2+} ; -⊞- Ag^+ ; -⊗- Tl^+ ; -●- Zn^{2+} ; -★- Cu^{2+} ; -⊠- Pb^{2+} ; -⊠- Cd^{2+} ; and -⊕- Hg^{2+} .

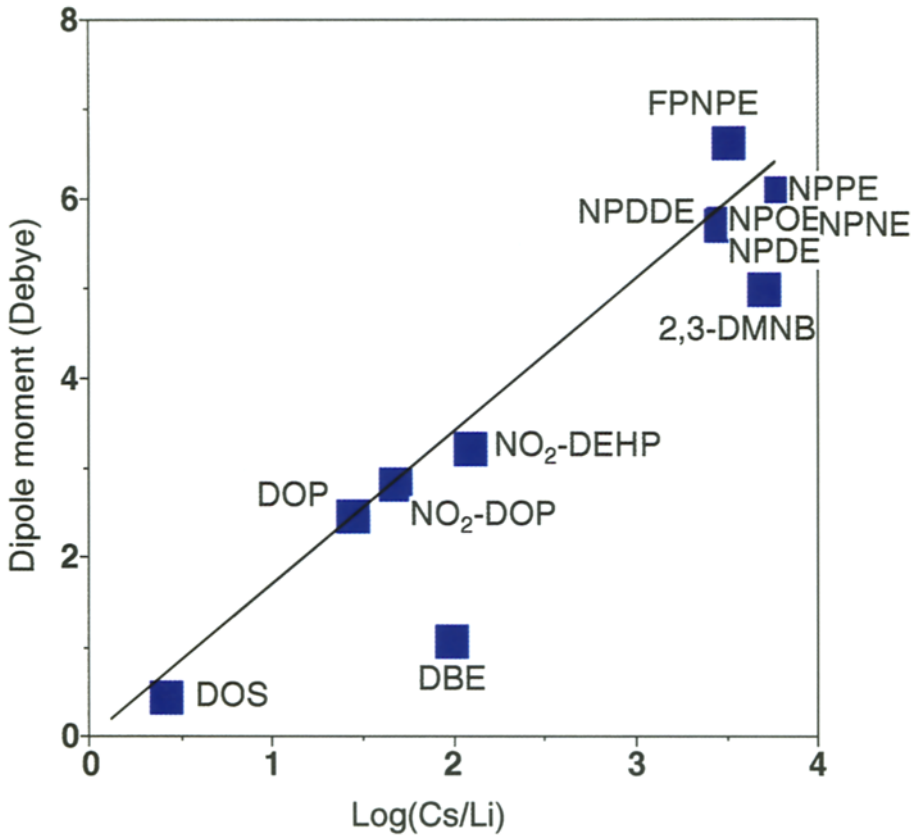


Fig. 2 Relation between cesium selectivity and dipole moment^{a)}

a) Calculated by MOPAC (PM3 method)

based on TEHP has a great affinity for 'hard' cations such as lithium. From these two factors, selectivity and sensitivity, it may be possible to say that FPNPE is a 'soft' plasticizer and TEHP is a 'hard' plasticizer.

Fiedler *et al.* investigated the potassium-selectivity change in a valinomycin system by mixing 2-NPOE and DEHA [7]. We assumed that an improvement of selectivity or specificity may be achieved by mixing two contrasting plasticizers; 'soft' FPNPE and 'hard' TEHP. Figure 5 shows the selectivity profiles obtained when the two plasticizers were mixed. It was shown that a continuous change in the affinity of the membrane to hard ions is possible by this method. It is very interesting that a reversal of selectivity takes place in the case of potassium, rubidium and cesium between 10% and 25% of TEHP, and in the case of lithium between 0% and 5%. This phenomenon is not well understood. TEHP which interacts strongly with lithium may play a crucial role as a lithium-selective ligand in the membrane.

TABLE I. Slopes of potential vs concentration curves for numerous cations [mV/decade].

ligand region ^a	FNDPE														
	no ligand			1			2			3			4		
	1-2	2-3	3-4	1-2	2-3	3-4	1-2	2-3	3-4	1-2	2-3	3-4	1-2	2-3	3-4
Tl ⁺	44	50	58	49	56	53	55	50	57	66	78	71	7	47	53
Ag ⁺	40	51	52	54	62	61	44	63	70	49	54	56	57	57	52
Hg ²⁺	–	3	52	–	29	58	–	6	87	–	0	23	–	43	74
Cs ⁺	53	57	55	49	54	50	57	55	40	54	56	59	51	55	54
Rb ⁺	54	56	56	50	56	52	48	40	42	55	55	64	54	55	51
K ⁺	55	57	54	52	57	54	53	50	57	45	58	58	51	53	53
Na ⁺	61	57	30	62	67	65	62	65	69	59	61	45	65	63	56
Li ⁺	51	52	22	63	48	42	52	55	53	72	53	22	29	66	37
NH ₄ ⁺	54	53	50	51	49	49	48	28	28	54	52	53	54	50	35
Mg ²⁺	52	32	29	44	35	34	47	35	24	49	42	14	58	21	18
Ca ²⁺	50	39	39	44	43	40	68	41	39	45	49	35	44	33	23
Ba ²⁺	40	39	41	42	37	42	87	43	28	42	41	41	42	49	36
Cu ²⁺	51	39	37	42	41	25	69	49	16	39	27	25	21	40	17
Pb ²⁺	17	31	36	52	41	37	38	40	41	39	38	34	27	46	41
Cd ²⁺	38	40	42	43	36	35	68	50	34	46	37	32	61	40	9
Zn ²⁺	39	37	25	43	31	40	89	24	14	70	38	30	59	47	10

ligand region ^a	TEHP														
	no ligand			1			2			3			4		
	1-2	2-3	3-4	1-2	2-3	3-4	1-2	2-3	3-4	1-2	2-3	3-4	1-2	2-3	3-4
Tl ⁺	51	58	54	52	50	49	48	56	42	48	53	47	44	54	59
Ag ⁺	56	61	53	59	58	64	54	65	65	54	45	48	62	59	56
Hg ²⁺	–	33	81	–	35	63	–	12	79	–	47	59	–	43	73
Cs ⁺	52	53	44	52	44	38	48	36	27	48	47	43	53	59	55
Rb ⁺	54	53	43	52	47	41	48	35	15	48	49	36	53	57	51
K ⁺	55	54	49	54	47	45	50	52	31	50	57	52	51	54	51
Na ⁺	71	67	56	60	63	60	59	68	69	59	57	51	68	55	56
Li ⁺	76	71	63	77	63	51	74	69	58	74	65	56	73	71	55
NH ₄ ⁺	57	55	57	55	48	49	54	54	41	54	52	42	53	54	48
Mg ²⁺	51	44	39	54	36	34	41	29	58	41	37	31	41	40	40
Ca ²⁺	34	42	40	48	39	37	41	33	28	41	37	31	46	40	29
Ba ²⁺	34	41	29	45	40	43	38	31	21	38	36	28	41	44	44
Cu ²⁺	72	62	43	69	44	43	78	64	35	78	52	31	72	51	38
Pb ²⁺	64	55	37	48	29	23	66	45	33	66	45	33	57	40	29
Cd ²⁺	52	43	43	47	34	48	57	36	25	57	38	31	47	37	21
Zn ²⁺	44	36	41	50	35	32	43	12	79	43	36	22	46	28	11

^a Figures show the region of concentration in sample solution; 1–2 means sensitivity between 10^{-1} and 10^{-2} mol/L.

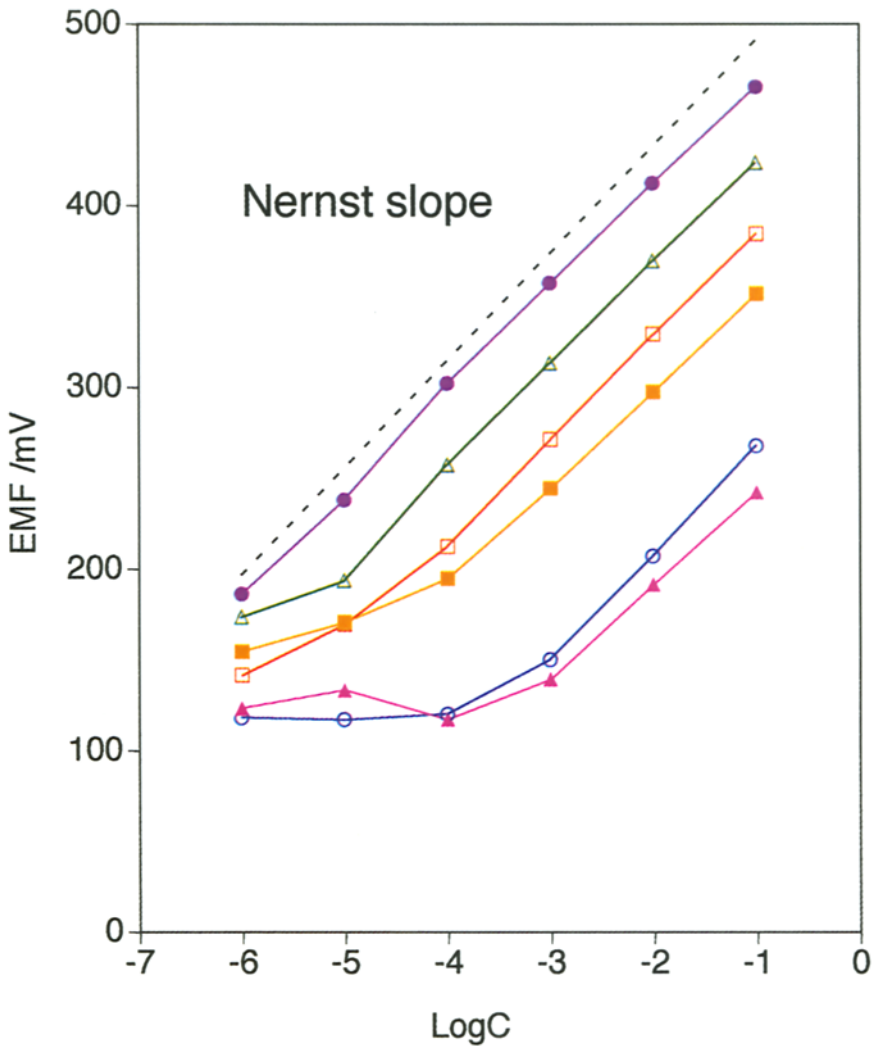


Fig. 3 Concentration dependence of potential (FPNPE);

-○- Na⁺; -□- K⁺; -△- Rb⁺; -●- Cs⁺; -■- NH₄⁺; and -▲- Li⁺.

The curve for ammonium ion does not intersect with that for sodium; this implies that it is impossible to treat the ammonium ion as one of the alkali metal cations.

Next, the value of cesium selectivity against lithium selectivity ($\log K_{\text{Cs}^+, \text{Li}^+}^{\text{pot}}$) without ligands estimated for each plasticizer from Figure 1, was adopted as the

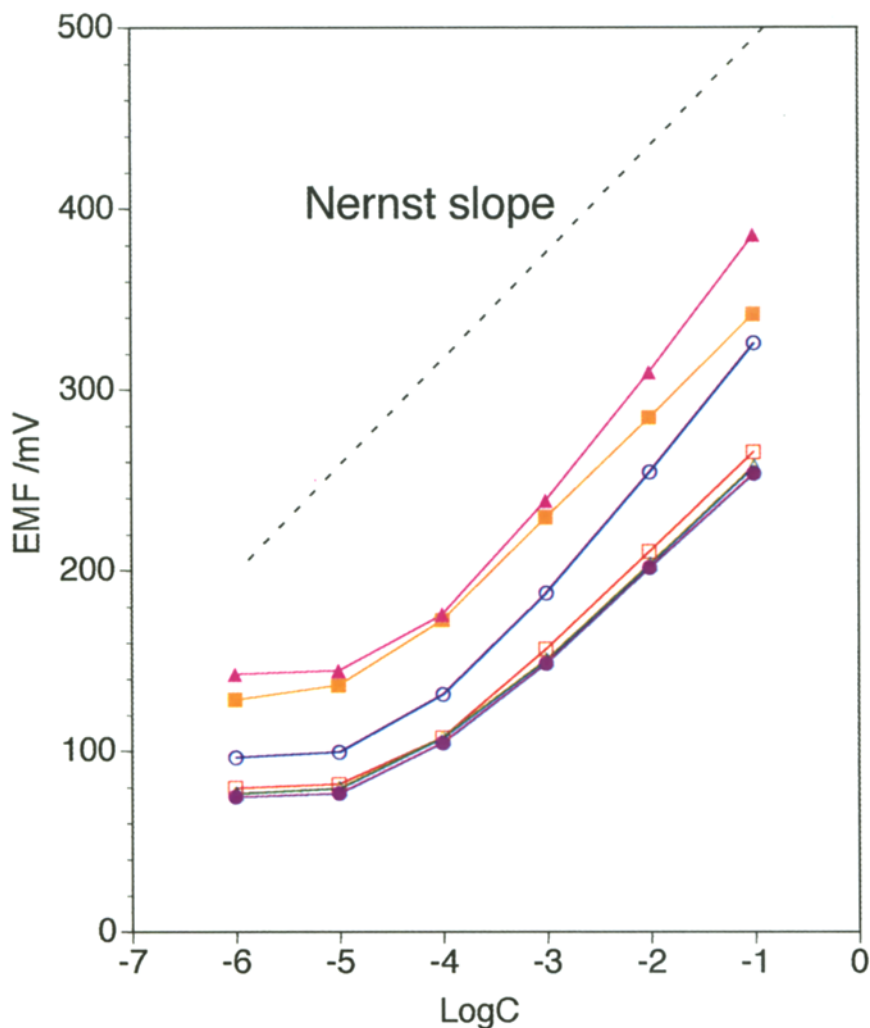


Fig. 4 Concentration dependence of potential (TEHP);

-○- Na⁺; -□- K⁺; -△- Rb⁺; -●- Cs⁺; -■- NH₄⁺; and -▲- Li⁺.

x axis, and sodium selectivity ($\log K_{Na^+, M^{n+}}^{pot}$, which has been determined using $10^{-3}M$ NaCl as a common inner solution) of several ligands was investigated. We expected that if a ligand is less affected by the environment, the selectivity may not be affected. The sensitivity value of each membrane is also summarized in Table I.

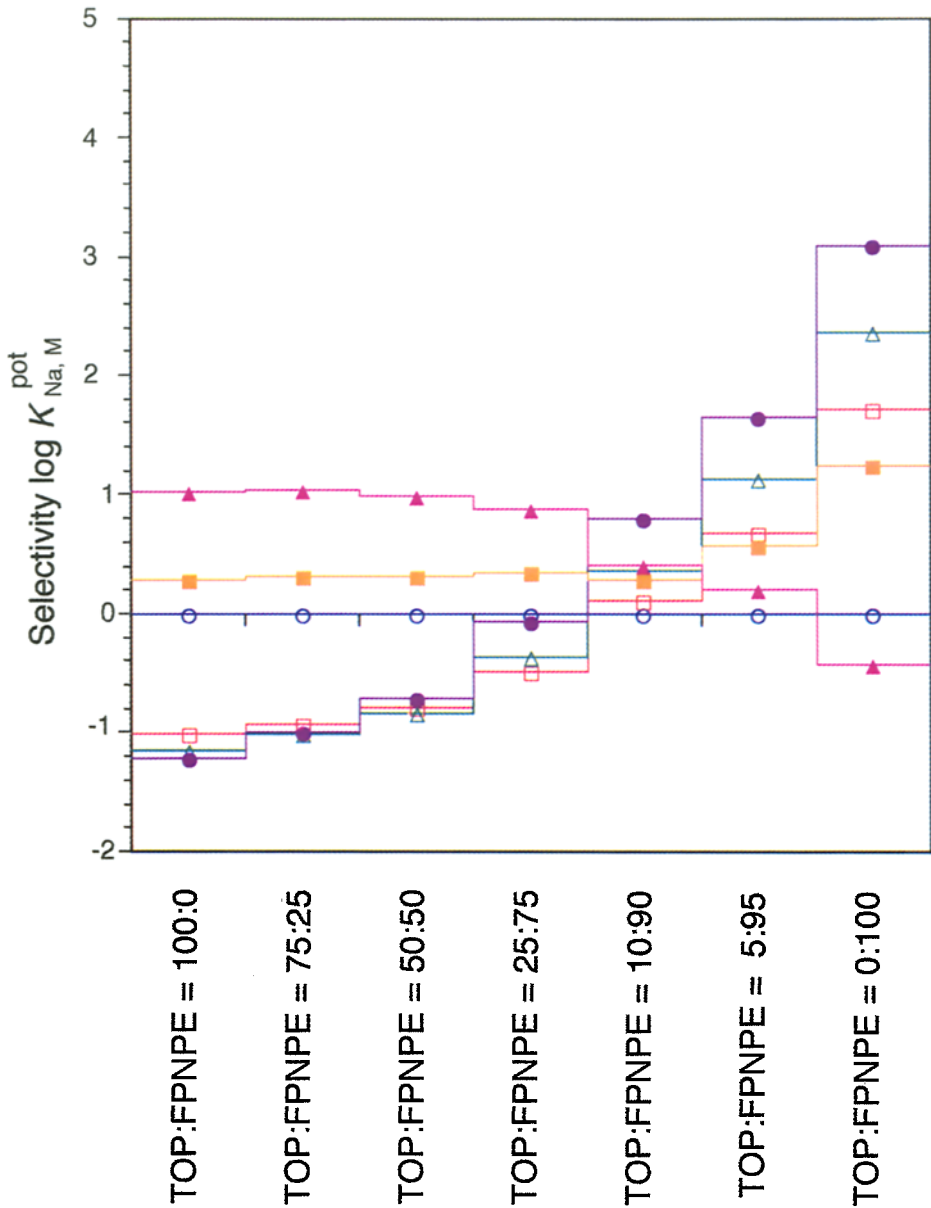


Fig. 5 Dependence of sodium selectivity on the ratio of mixed plasticizers; -○- Na^+ ; -□- K^+ ; -△- Rb^+ ; -●- Cs^+ ; -■- NH_4^+ ; and -▲- Li^+ .

The selectivity profile of bis(12-crown-4) (**1**) is summarized in Figure 6. As can be seen from the figure, a small selectivity change was observed for large cations such as potassium, rubidium and cesium. This indicates that the ionophoric cavity is firmly maintained in the membrane. By contrast, a large selectivity change took place for relatively small ions such as lithium, zinc and cuprous, especially in the minus region on the x axis. We think that this is due to the environmental effect of hard plasticizers because size selectivity is less effective for the smaller ions compared to the cavity size of the host molecules. It seems difficult for strongly hydrated lithium ion to be transferred from the aqueous phase to the plasticizer phase with 'softness'.

Selectivity profiles of *p*-tert-octylcalix[4]arene tetraethyl ester (**2**) are summarized in Figure 7. The effect of a plasticizer on divalent cations was larger than that in bis(12-crown-4). As tetrahedral ammonium ion interacts with the cavity of calix[4]arene tetraethyl ester only weakly, the change in the selectivity appears very marked. On the other hand, the change in potassium and cesium selectivity remained rather small.

The selectivity profiles of 25,26,27,28-tetrakis(phenoxyethoxy)-*p*-tert-butylcalix[4]arene (**3**) is summarized in Figure 8. The selectivity for all cations except ammonium ion is changed drastically. In particular, the selectivity change towards so-called soft cations such as Cs^+ , Tl^+ and Hg^{2+} was very large [12]. This ligand showed high Tl^+ selectivity when 100% of FPNPE was used as a plasticizer. The most interesting point in this ligand is observed for divalent cations. They showed a maximum point at around $\log(\text{Cs}/\text{Li}) = 0$. The fact indicates that the selectivity for divalent cations is influenced by two different factors. It is an acceptable idea that when the lipophilicity of the membrane without ligand is very high, it is difficult for the divalent ions to be transferred from the aqueous phase to the membrane phase as a result of the environment effect. On the other hand, it is not easy to explain the left side of the curves: we now consider that the magnitude of the contribution to the response due to the plasticizer was large because host **3** would have a weaker complexing ability as compared to the other three hosts.

p-tert-Butylcalix[6]arene hexaethyl ester (**4**) was investigated and the results are summarized in Figure 9. For lithium and cuprous, a similar phenomenon was observed as the case in bis(12-crown-4). This ligand showed cesium selectivity when FPNPE is used as a plasticizer, but the change in the selectivity remained small. This fact shows that this ligand stably maintains an ionophoric cavity in the membrane. These results consistently indicate that the mixed plasticizer method allows us to estimate the characteristic behavior of the ligand in a membrane, as well as those of the individual ion.

4. Conclusions

The present study demonstrates a versatile guide for the selection of plasticizers. In general, when a neutral carrier which firmly retains an ionophoric cavity in the

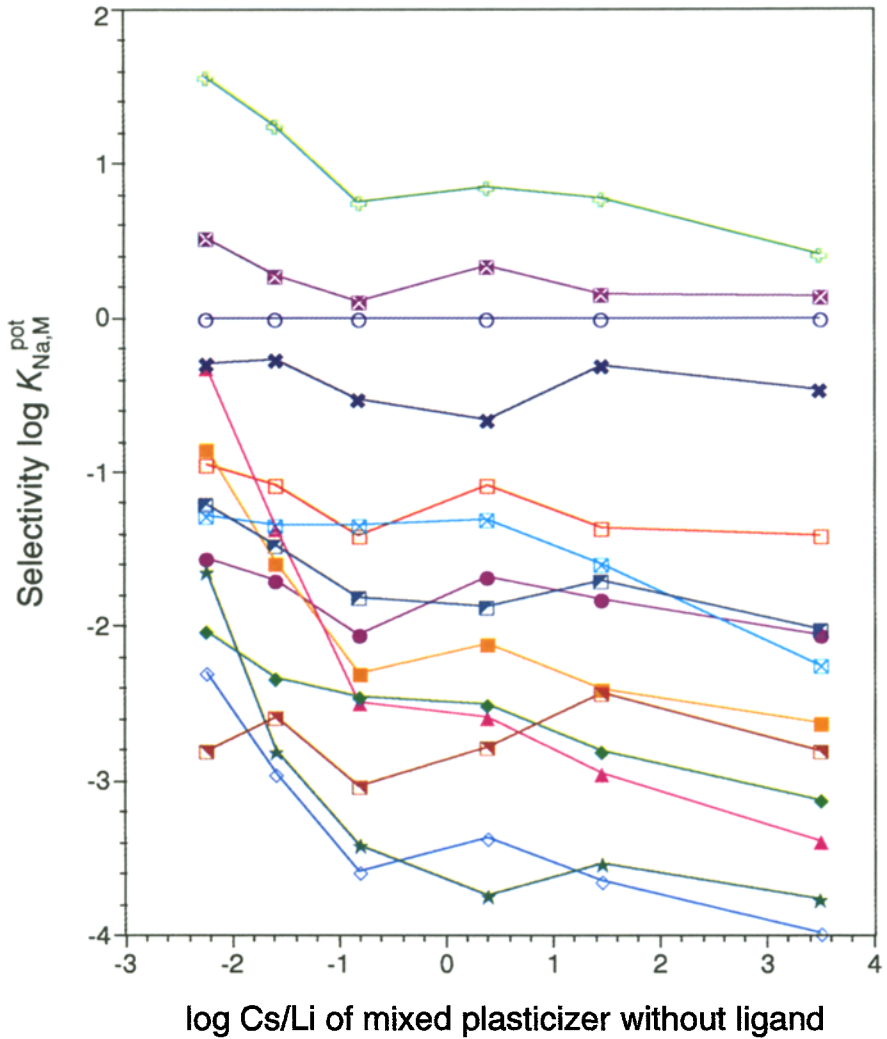


Fig. 6 Selectivity profiles of ligand 1; -○- Na⁺; -□- K⁺;
 -●- Cs⁺; -■- NH₄⁺; -▲- Li⁺; -◇- Mg²⁺; -◆- Ca²⁺; -⊠- Ba²⁺;
 -⊠- Ag⁺; -⊠- Tl⁺; -★- Cu²⁺; -▣- Pb²⁺; -▣- Cd²⁺; and -⊕- Hg²⁺.

(Plots of Rb⁺ and Zn²⁺ were omitted to make the figure understandable. Rb⁺ existed almost in the middle between K⁺ and Cs⁺. Plots of Zn²⁺ were almost identical to those of Mg²⁺.)

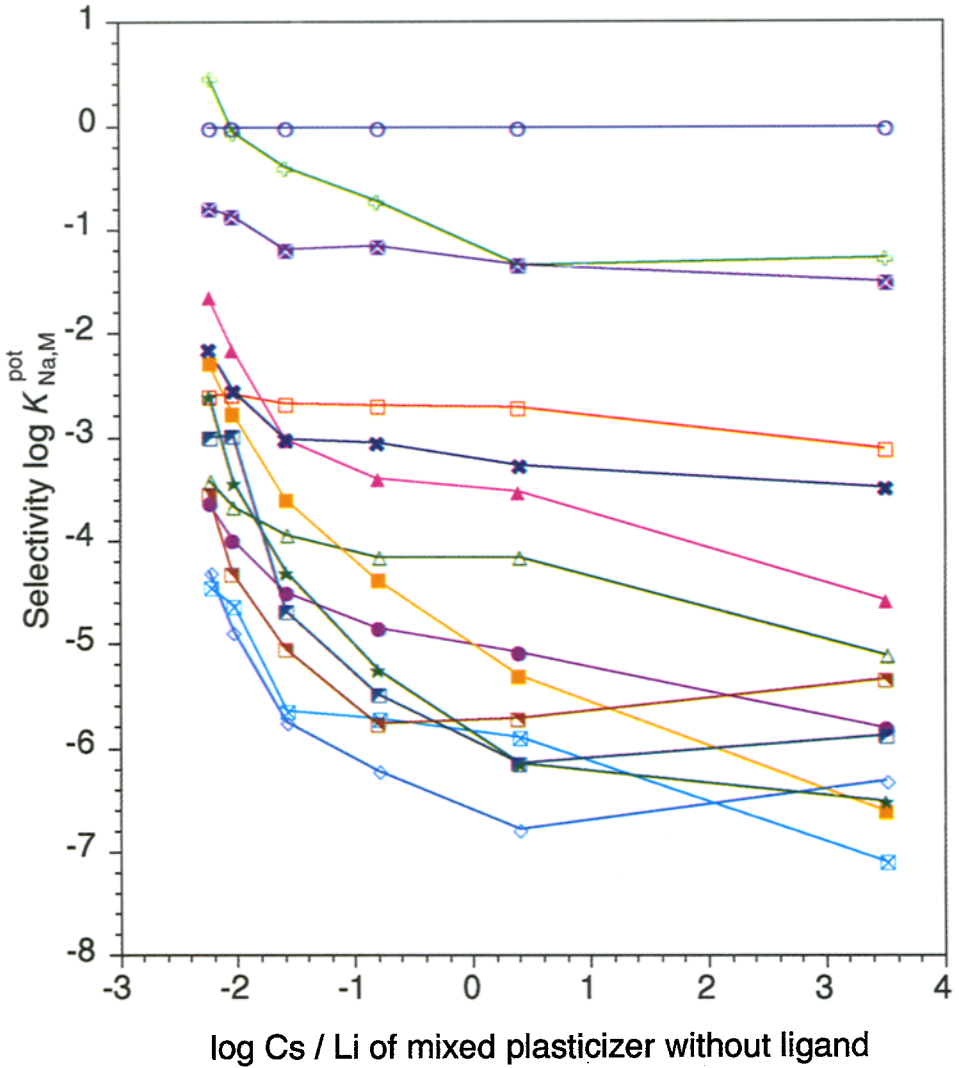


Fig. 7 Selectivity profiles of **2**; -O- Na⁺; -□- K⁺; -△- Rb⁺; -●- Cs⁺; -■- NH₄⁺; -▲- Li⁺; -◇- Mg²⁺; -⊠- Ba²⁺; -⊗- Ag⁺; -⊠- Tl⁺; -★- Cu²⁺; -▣- Pb²⁺; -▤- Cd²⁺; and -⊕- Hg²⁺. (Plots of Ca²⁺ and Zn²⁺ were omitted. They existed in the region between Cs⁺ and Mg²⁺.)

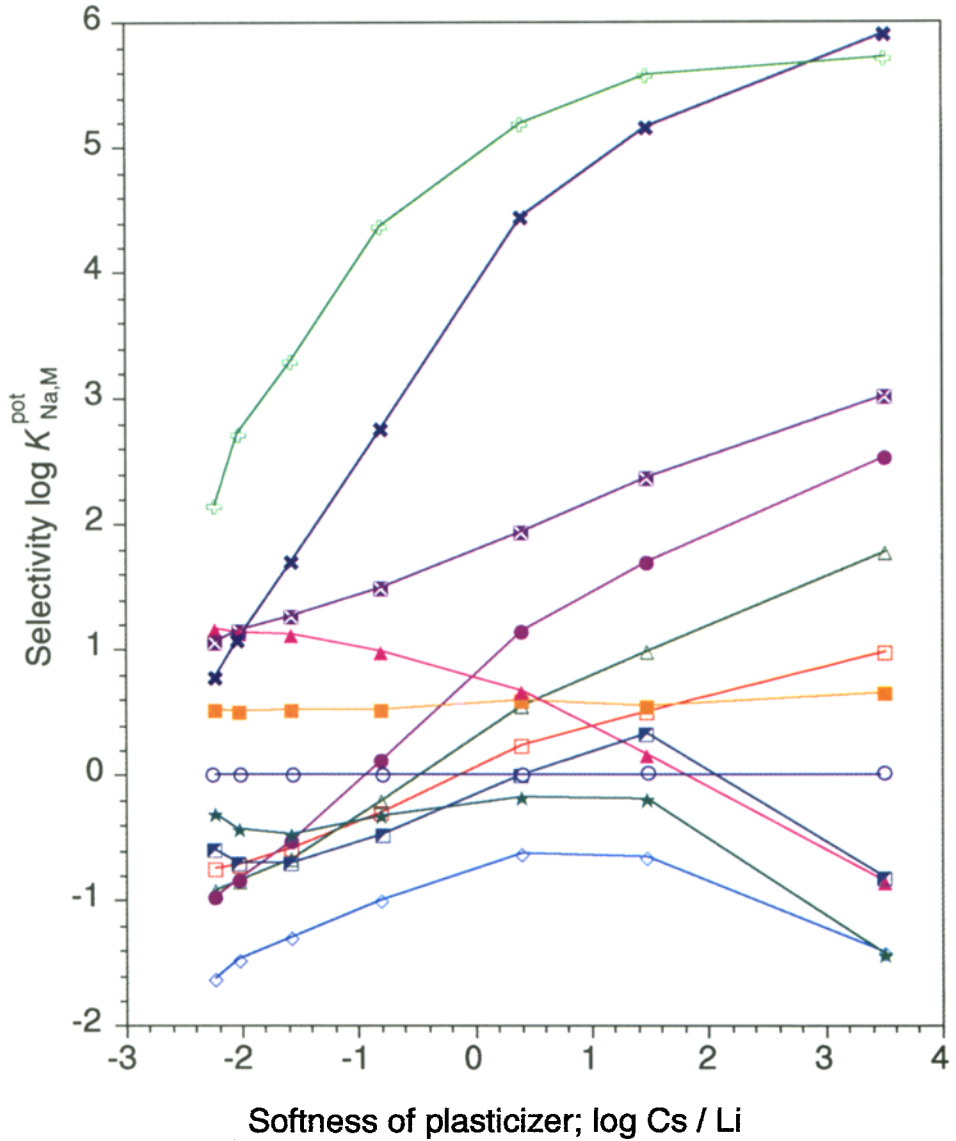


Fig. 8 Selectivity profiles of 3; -○- Na^+ ; -□- K^+ ; -△- Rb^+ ; -●- Cs^+ ; -■- NH_4^+ ; -▲- Li^+ ; -◇- Mg^{2+} ; -×- Ag^+ ; -* - Tl^+ ; -★- Cu^{2+} ; -▣- Pb^{2+} ; and -⊕- Hg^{2+} .

(Plots of Ca^{2+} , Ba^{2+} , Zn^{2+} , and Cd^{2+} were omitted. They existed in the region between Pb^{2+} and Mg^{2+} with the same tendency.)

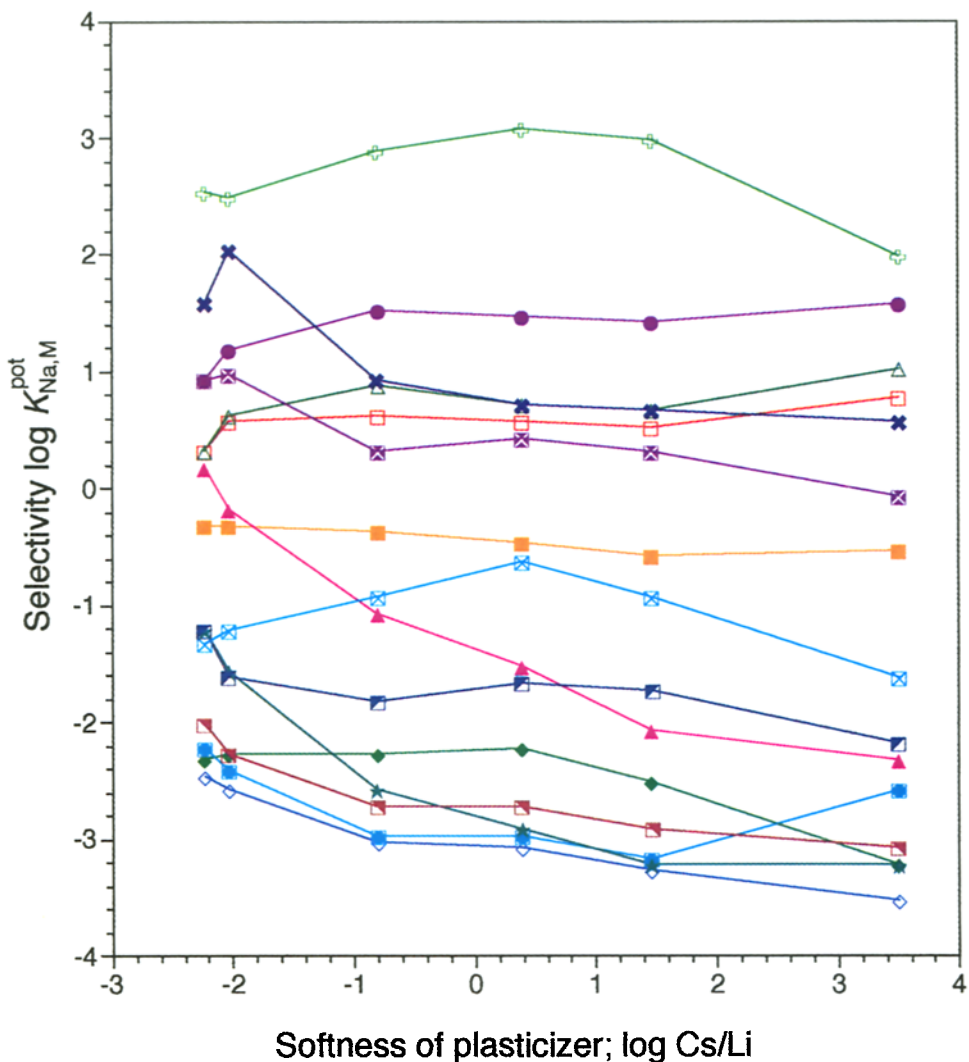


Fig. 9 Sodium selectivity profiles of *p-tert*-butylcalix[6]arene hexaethyl ester; -○- Na⁺; -□- K⁺; -△- Rb⁺; -●- Cs⁺; -■- NH₄⁺; -▲- Li⁺; -◇- Mg²⁺; -◆- Ca²⁺; -⊠- Ba²⁺; -⊗- Ag⁺; -✱- Tl⁺; -★- Cu²⁺; -▣- Pb²⁺; and -⊕- Hg²⁺.

(Plots of Zn²⁺ and Cd²⁺ were omitted. Zn²⁺ and Cd²⁺ behaved almost in the same manner as Mg²⁺.)

membrane phase is used, the ion selectivity is less affected by the change in the plasticizer. In contrast, when a neutral carrier which has a flexible metal-binding site is used, the ion selectivity is remarkably affected by the nature of the plasticizer. Although a few exceptions exist, we can generalize the trend as follows: the 'soft' plasticizer with a high dipole moment (*e.g.*, FPNPE) is recommended when the interfering metal ion is 'hard' (*e.g.*, Li^+) whereas the 'hard' plasticizer (*e.g.*, TEHP) is recommended when the interfering metal ion is 'soft' (*e.g.*, Cs^+). We believe that the present study is useful when choosing an appropriate plasticizer for ion-selective electrodes which show high metal selectivity.

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