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Molecular Design of Calixarene-Based Ion-Selective Electrodes

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Abstract. In order to obtain insights into relationships between the calix[4]arene structure and the ion selectivity in the electrode system, 20 ionophoric calix[4]arenes were synthesized and their ion selectivity (with Na^+ as a standard) estimated. Among these ionophoric calix[4]arenes, 25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]-*p*-t-octylcalix[4]arene afforded the highest log $K^{pot}_{Na,M}$ value (-3.1) in the presence of 2-fluorophenyl-2′-nitrophenylether (**10**) as the best of 13 plasticizers. This is the first example in which the Na^+/K^+ selectivity exceeds a factor of 10^3 in the electrode system based on the neutral carrier. The high Na^+ selectivity is attributed to modification of the upper rim which ostensibly has no relation with the component of the cavity. This paper demonstrates the potential relationships between the unique structure of the calix[4]arene-based ligands and selectivity performance for the design of ion-selective electrodes.

Key words. Calixarenes, ion-selective electrodes, Na^+ selectivity.

1. Introduction

Macrocyclic compounds were successfully applied for the first time to ion-selective electrodes by Simon [1]. He succeeded in the design of a K^+-selective electrode by the use of valinomycin which can be extracted from *Streptomyces fulvissimus* [2]. Subsequently, he designed a variety of ion-selective electrodes using noncyclic ionophores and obtained some insights into a relationship between the structure and the selectivity [3]. Ion-selective electrodes were also made from crown ethers, which were discovered by Pedersen [4]. At the beginning of the research, however, crown ether-based electrodes did not show any high ion selectivity. The electrode that shows practical ion selectivity was made by Shono *et al.* [5] by using bis(benzo-15-crown-5) ethers. The ion-selective electrode in a poly(vinyl chloride) (PVC)-plasticizer system was further improved through several additional findings, such as tetraphenyl borate as an additive and *o*-nitrophenyl octyl ether (**11**) as a plasticizer. It is now known, however, that the crown ether-based electrode is hampered by the flexibility of the ring and the induced-fit nature. It thus seems to be difficult to improve the ion selectivity further. To the best of our knowledge, the highest ion selectivity achieved so far is 5×10^3 for K^+ (against Na^+) and about 1×10^2 for Na^+ (against K^+).

Calix[*n*]arenes, the synthetic method for which was established by Gutsche [6, 7], are cyclic oligomers made up of phenol and formaldehyde. In contrast to flexible

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crown ether rings, those of calix[*n*]arenes are more rigid. It is known that conformationally immobilized calix[4]arenes are particularly rigid and the cone isomer is particularly suitable as a basic skeleton for the design of ion sensors. Diamond and McKervey's group introduced $-CH_2COR$, $-CH_2COOR$ and $-CH_2CONR_2$ groups into the OH groups on the lower rim and demonstrated that they have an Na^+ selectivity higher than that attained in crown compounds [8]. They have already applied these calixarene-based ionophores to the design of ion-selective electrodes [9–15]; in contrast K. Kimura *et al.* have achieved high Na^+ selectivity by incorporating long alkyl chains into the acetate ester [16].

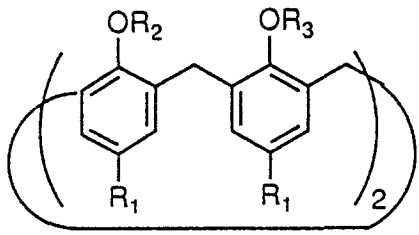
Recently, Shono *et al.* reported that de-t-butylation leads to the loss of the fine selectivity although no modification was performed around the ionophoric ester cavity [17]. We considered that to attain a high ion selectivity in the electrode system, one should pay more attention not only to the ionophore but also to the 'environmental' conditions. This view is supported by the fact that the ion selectivity of crown compounds is generally low in dibutyl phthalate (as a plasticizer), which has a low dielectric constant, whereas it is significantly improved in **11**, which has a high dielectric constant [18]. In order to obtain insights into the relationship between the calixarene structure and the ion selectivity and that between the 'environmental' conditions and the ion selectivity, we have designed the electrodes from 20 calixarene-based ionophores in the presence of 13 plasticizers. We finally found that a *p*-t-octylcalix[4]aryl ester with a cone conformation can show the highest Na^+ selectivity ($10^{3.1}$ against K^+) achieved so far.

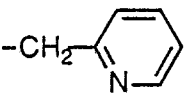
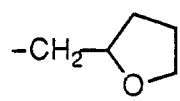
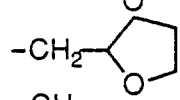
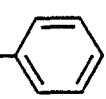
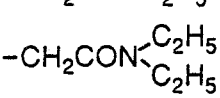
2. Experimental

2.1. SYNTHESIS

2.1.1. *Cone*-**1**(*4EtOPr*)

p-t-Butylcalix[4]arene (2.2 g, 3.0 mmol), sodium hydride (60% in oil, 1.1 g, 27 mmol) and potassium iodide (0.32 g, 1.9 mmol) were dissolved in *N*,*N*-dimethylformamide (DMF, 100 mL) and the solution was stirred for 30 min at room temperature. After chloroethyl propyl ether (13 g, 0.11 mol) was added, the reaction was continued under stirring for 96 h at 80°C. After cooling, the solution was poured into carbon dioxide-saturated water (500 mL). The solution was extracted with chloroform (150 mL) and the organic layer was separated, filtered and concentrated *in vacuo*. Chromatographic separation on silica gel with chloroform-toluene (1:3 v/v) as eluent yielded 25,26,27,28-tetrakis(propoxyethoxy)-*p*-t-butylcalix[4]arene with a cone conformation, cone-**1**(4EtOPr) (0.95 g, 32%) as white crystals; m.p. 106–108°C (from methanol); ν_{max} (KBr)/cm^{-1} 2961 (C—H), 1481 (Ar), 1201 (CH_2O); δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 0.928 (12H, *t*, *J* 7.7, CH_2CH_3), 1.07 (36H, *s*, Bu^t), 1.63 (8H, *dt*, *J* 7.7, *J* 6, CCH_2Me), 3.10, 4.44 (4H each, H_{AB}, *J* 13 each, $ArCH_2Ar$), 3.47 (8H, *t*, *J* 6, OCH_2Et), 3.88–4.16 (16H, *m*, OCH_2CH_2O), 6.77 (8H, *s*, ArH); *Found*: C, 77.39; H, 9.68. *Calcd.* for $C_{64}H_{96}O_8$: C, 77.38; H, 9.74%.



R_1	R_2 , R_3	
t-Butyl	$-CH_2COOC_2H_5$, 	1(2Es2Py)
〃	$-CH_2COOC_2H_5$	1(4Es)
〃	$-C_2H_4OC_2H_5$	1(4EtOEt)
〃	$-CH_2OCH_3$	1(4MeOMe)
〃	$-C_2H_4OC_3H_7$	1(4EtOPr)
〃		1(4Fu)
〃	 , $-CH_2COOC_2H_5$	1(2Fu2Es)
〃	 , $-H$	1(2Fu2OH)
〃	$-CH_3$, $-H$	1(2Me2OH)
〃	$-CH_2OCH_3$, $-H$	1(2MeOMe2OH)
〃		1(4EtOPh)
〃	$-CH_3$, $-CH_2COOC_2H_5$	1(2Me2Es)
〃	$-CH_3$, 	1(2Me2Am)
〃	$-CH_3$	1(4Me)
〃	$-C_3H_7$	1(4Pr)
Octadecyl	$-CH_2COOC_2H_5$	**2**(4Es)
t-Octyl	$-CH_2COOC_2H_5$	**3**(4Es)

2.1.2. *Cone*-**1**(*2Fu2OH*) *and Cone*-**1**(*4Fu*)

The same procedure as described above yielded 25,27-bis(tetrahydrofurfuryloxy)-26,28-dihydroxy-*p*-t-butylcalix[4]arene [cone-**1**(2Fu-2OH)] as a mixture of *R*,*S*-, *R*,*R*- and *S*,*S*-stereoisomers (1.0 g, 41%); m.p. 107–109°C; ν_{max} (KBr)/cm^{-1} 3300 (OH), 1485 (Ar), 1198 (CH_2O); δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 0.99–1.20 (36H, *m*, Bu^t), 1.90–2.03 (8H, *m*, CCH_2C), 4.44, 3.27 (4H each, H_{AB}, *J* 13 each, $ArCH_2Ar$), 3.89–4.00 (10H, *m*, OCH); *Found*: C, 79.41; H, 8.84. *Calcd.* for $C_{54}H_{72}O_6$: C, 79.37; H, 8.88% and 25,26,27,28-tetrakis(tetrahydrofurfuryloxy)-*p*-t-butylcalix[4]arene with a cone conformation [cone-**1**(4Fu)], as a mixture of *R*,*R*,*R*,*R*- and *S*,*S*,*S*,*S*-stereoisomers (0.12 g, 4.1%); m.p. 152–155°C; ν_{max} (KBr)/cm^{-1} 2950 (CH), 1480 (Ar), 1205 (CH_2O); δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 1.07 (36H, *s*, Bu^t), 1.65–2.10 (16H, *br m*, CCH_2C), 3.13 (4H, H_{AB}, *J* 13 ArCHAr), 3.70–4.75 (24H, *br m*, OCH and ArCHAr), 6.78 (8H, *s*, ArH); *Found*: C, 78.07; H, 8.89. *Calcd.* for $C_{64}H_{88}O_8$: C, 78.01; H, 9.00%.

2.1.3. *Cone*-**1**(*2Fu2Es*)

1(2Fu2OH) (0.5 g, 0.61 mmol), ethylbromoacetate (2.4 g, 15 mmol) and sodium hydride (60% in oil, 0.24 g, 15 mmol) were mixed in THF (40 mL) under a nitrogen stream. The mixture was refluxed for 48 h. After cooling, the mixture was poured into carbon dioxide-saturated water (300 mL). The crude product was extracted with chloroform (50 mL) twice. The resultant chloroform solution was filtered, dried and concentrated under reduced pressure to remove excess ethyl bromoacetate. The chromatographic separation on silica gel with chloroform–toluene (1 : 3 v/v) as eluent yielded 25,27-bis(furfuryloxy)-26,28-[(ethoxycarbonyl)methoxy]-*p*-t-butylcalix[4]arene with a cone conformation, cone-**1**(2Fu2Es) as white crystals (0.29 g, 48%); m.p. 203–204°C (from acetone); ν_{max} (KBr)/cm^{-1} 2861 (C—H), 1763 (C=O), 1482 (Ar), 1129 (CH_2O); δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 1.06 (36H each, *br s*, Bu^t), 1.27 (6H, *t*, *J* 7, CH_2CH_3), 1.40–1.95 (8H, *m*, CH_2CH_2C), 3.13 (4H, H_{AB}, *J* 13, ArCHAr), 3.65–4.80 (36H, *m*, OCH_2CO, ArCHAr, OCH_2CH_2, $OCHCH_2$), 4.20 (4H, *q*, *J* 7, OCH_2CH_3), 6.75, 6.79 (4H each, *s* each, ArH); *Found*: C, 75.27; H, 8.60. *Calcd.* for $C_{62}H_{84}O_{10}$: C, 75.27; H, 8.56%.

2.1.4. *Cone*-**1**(*2MeOMe2OH*)

p-t-Butylcalix[4]arene (2.2 g, 3.0 mmol) and trimethylbenzylammonium chloride (0.56 g, 3.0 mmol) were dissolved in dichloromethane (5.0 mL) and NaOH (5.0 g, 0.12 mol) was dissolved in water (4.8 mL). To the mixture of these two solutions chloromethyl methyl ether (0.72 g, 9 mmol) was added dropwise and the reaction was continued under stirring at 0°C for 4 h and then at room temperature for 2 h. Water (200 mL) and dichlormethane (50 mL) were added and the aqueous phase was neutralized with dil. HCl. The organic layer was separated and concentrated *in vacuo*. The resultant crude product was recrystallized from acetone to give 25,27-bis(methoxymethoxy)-26,28-dihydroxy-*p*-t-butylcalix[4]arene [cone-**1**(2MeOMe2OH)] as white crystals (1.8 g, 80%); m.p. 225–228°C; ν_{max} (KBr)/cm^{-1} 3316 (OH),

2963 (CH), 1487 (Ar), 1157 (CH_2O); δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 0.93, 1.30 (36H, *s* each, Bu^t), 3.33, 4.32 (4H each, H_{AB}, *J* 14 each, $ArCH_2Ar$), 3.74 (6H, *s*, OCH_3), 5.14 (4H, *s*, OCH_2O), 6.76, 7.07 (4H each, *s* each, ArH), 6.79 (2H, *s*, OH); *Found*: C, 78.31; H, 8.69. *Calcd.* for $C_{48}H_{64}O_6$: C, 78.22; H, 8.75%.

2.1.5. *Cone*-**1**(*4MeOMe*)

25,26,27,28-Tetrakis(methoxymethoxy)-*p*-t-butylcalix[4]arene with a cone conformation, cone-**1**(4MeOMe) was synthesized in a manner similar to that described above except two points: 25 times of chloromethyl methyl ether (6.0 g, 75 mmol) were used and the reaction time was prolonged to 24 h at room temperature; white crystals (0.75 g, 30%); m.p. 182–184°C; ν_{max} (KBr)/cm^{-1} 2961 (CH), 1485 (Ar), 1121 (CH_2O); δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 1.08 (36H, *s*, Bu^t), 3.19, 4.48 (4H each, H_{AB}, *J* 13 each, $ArCH_2Ar$), 3.63 (12H, *s*, OCH_3), 5.13 (8H, *s*, OCH_2O), 6.79 (8H, *s*, ArH); *Found*: C, 74.85; H, 8.81. *Calcd.* for $C_{52}H_{72}O_8$: C, 75.69; H 8.80%.

2.1.6. **1**(*2Me2OH*)

p-t-Butylcalix[4]arene (2.0 g, 2.7 mmol), methyl iodide (3.8 g, 27 mmol) and potassium carbonate (0.75 g, 5.4 mmol) were mixed in dry acetone (50 mL) and the mixture was refluxed under a nitrogen atmosphere for 24 h. After cooling, 1 mol dm^{-3} aqueous hydrochloric acid (50 mL) was added. The resultant white precipitate was extracted with chloroform (100 mL). After washing the organic layer with water (50 mL) three times, the organic layer was separated, dried over magnesium sulfate and concentrated under reduced pressure. The residue was recrystallized from chloroform-methanol (1 : 9 v/v) to give 25,27-dimethoxy-26,28-dihydroxy-*p*-t-butylcalix[4]arene [**1**(2Me2OH)] as a white powder (1.4 g, 77%); m.p. 252–254°C; ν_{max} (KBr)/cm^{-1} 3360 (OH), δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 0.83, 0.92 (18H each, *s* each, Bu^t), 3.31, 4.29 (4H each, *d* each, $ArCH_2Ar$), 3.94 (6H, *s*, CH_3), 6.75, 7.07 (4H each, *s* each, ArH), 7.11 (2H, *s*, OH); *Found*: C, 81.53; H, 9.06. *Calcd.* for $C_{46}H_{60}O_4$: C, 81.61; H, 8.93%.

2.1.7. **1**(*2Me2Am*)

Compound **1**(2Me2OH) (1.0 g, 1.5 mmol), 2-chloro-*N*,*N*-diethylacetamide (1.1 g, 7.4 mmol) and sodium hydride (60% in oil, 0.30 g, 7.4 mmol) were mixed in THF (40 mL) under a nitrogen stream. The mixture was refluxed for 12 h. After cooling, water (300 mL) and dichloromethane (50 mL) were added and the resultant mixture was shaken over 100 times to extract the product into the organic phase. The organic layer was separated and the aqueous layer was extracted again with dichloromethane (50 mL). The two dichlormethane solutions were combined and washed twice with water (25 mL), dried over magnesium sulfate and concentrated *in vacuo*. The chromatographic separation on silica gel with chloroform-benzene (1 : 1 v/v) as eluent yielded 25,27-bis(*N*,*N*-diethylamidomethoxy)-26,28-dimethoxy-*p*-t-butylcalix[4]arene as a white powder (1.0 g, 75%); m.p. 82–84°C; ν_{max} (KBr)/cm^{-1} 1650 (C=O); δ_H (90 MHz, CD_3SOCD_3, 100°C, DSS) 0.85, 1.25 (18H each,

s each, Bu^t), 1.05 (6H, *t*, *J* 7, CH_2CH_3), 3.16 (4H, H_{AB}, *J* 13, ArCHAr), 3.23 (4H, *q*, *J* 7, CH_2CH_3), 4.11 (4H, H_{AB}, *J* 13, ArCHAr), 3.32 (4H, *s*, OCH_2CO), 6.49 and 7.09 (4H each, *s* each, ArH); *Found*: C, 76.92; H, 9.08; N, 3.00. *Calcd.* for $C_{58}H_{82}O_6N_2$: C, 77.12; H, 9.15; N, 3.10%.

2.1.8. **1**(*4EtOPh*)

p-t-Butylcalix[4]arene (2.0 g, 2.7 mmol), sodium hydride (60% in oil, 1.1 g, 27 mmol) and potassium iodide (0.32 g, 1.9 mmol) were added to *N*,*N*-dimethylformamide (100 mL) and the mixture was stirred for 30 min. After 2-chloroethyl phenyl ether (17 g, 0.11 mol) was added, the mixture was stirred for 4 days at 80°C. After cooling, water (300 mL) and dichloromethane (50 mL) were added. The resultant mixture was shaken over 100 times to extract the product into the organic phase. The organic layer was separated and the aqueous phase was extracted again with dichloromethane (50 mL). The two dichloromethane solutions were combined and washed twice with water (25 mL), dried over magnesium sulfate and concentrated *in vacuo*. The chromatographic separation on silica gel with benzene-chloroform (1 : 1 v/v) as eluent yielded 25,26,27,28-tetrakis(phenoxyethoxy)-*p*-t-butylcalix[4]arene with a cone conformation, cone-**1**(4EtOPh) as white powder (0.61 g, 18%); m.p. 143–145°C; ν_{max} (KBr)/cm^{-1} 2963 (CH), 1601 (Ar), 1246 (CH_2O); δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 1.08 (36H, *s*, Bu^t), 3.14, 4.09 (4H each, H_{AB}, *J* 13 each, $ArCH_2Ar$), 4.29 (16H, *s*, OCH_2CH_2O), 6.76–7.25 (28H, *m*, ArH); *Found*: C, 80.79; H, 7.81. *Calcd.* for $C_{76}H_{88}O_8$: C, 80.82; H, 7.85%.

2.1.9. *Cone*-**2**(*4Es*)

p-t-Octylcalix[4]arene (1.0 g, 1.1 mmol), ethyl bromoacetate (4.4 g, 26 mmol) and potassium carbonate (3.6 g, 26 mmol) were mixed in dry acetone (60 mL). The mixture was refluxed for 16 h under a nitrogen atmosphere. After cooling, the mixture was poured into carbon dioxide-saturated water (500 mL). The crude product was extracted with chloroform (50 mL) twice. The resultant chloroform solution was filtered, dried and concentrated under reduced pressure to remove excess ethyl bromoacetate. The resultant viscous liquid was crystallized from 2-propanol to give 25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]-*p*-t-octylcalix[4]arene with a cone conformation, cone-**2**(4Es) as white crystals (0.75 g, 54%); m.p. 144–145°C; ν_{max} (KBr)/cm^{-1} 2957, 2917, 2850 (CH each), 1757 (C=O), 1473 (Ar); δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 0.70 [12H, *s*, $C(CH_3)_2CH_2(CH_3)_3$], 1.01 [24H, *s*, $C(CH_3)_2CH_2(CH_3)_3$], 1.55 [8H, *s*, $C(CH_3)_2CH_2(CH_3)_3$], 1.26 (12H, *t*, *J* 7, CH_2CH_3), 3.18 (4H, H_{AB}, *J* 14, ArCHAr), 4.19 (8H, *q*, *J* 7, CH_2CH_3), 4.78 (8H, *s*, OCH_2CO), 4.80 (4H, H_{AB}, *J* 14, ArCHAr), 6.75 (8H, *s*, ArH); *Found*: C, 74.67; H, 9.30. *Calcd.* for $C_{76}H_{112}O_{12}$: C, 74.96; H, 9.27%.

2.1.10. *Cone*-**3**(*4Es*)

This compound was synthesized via three steps.

(a) *p-Dodecanoylcalix*[4]*arene*. *n*-Dodecanoyl chloride (13.6 g, 62 mmol) and ground $AlCl_3$ (8.3 g, 62 mmol) were mixed in nitrobenzene (180 mL) and the

mixture was stirred for 30 min at room temperature under a nitrogen atmosphere. *p*-t-Butyl-calix[4]arene (11.9 g, 16 mmol) was added and the mixture was stirred at 60°C for 11 h and then at 70°C for 3 h. After cooling, the reaction mixture was poured into 1 mol dm^{-3} HCl solution (1200 mL) and the product was extracted with chloroform. The organic layer was separated, washed with water and dried over magnesium sulfate. The solution was concentrated, the residue being precipitated from chloroform–methanol to give the pale brown solid. The crude product thus obtained was recrystallized from benzene–methanol to give *p*-dodecanoylcalix[4]arene (14 g, 76%) as a brown powder; m.p. 142–143°C; ν_{max} (KBr)/cm^{-1} 3188 (OH), 2918, 2849 (CH each), 1676 (C=O), 1605 (Ar), 1466 (C=O), 1321; δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 0.87 (12H, *br t*, CH_3), 1.26 [32H, *s*, $CH_2CH_2(CH_2)_8CH_3$], 1.58 [8H, *br*, $CH_2CH_2(CH_2)_8CH_3$], 2.82 [8H, *br t*, $CH_2CH_2(CH_2)_8CH_3$], 4.01 (8H, *br s*, $ArCH_2Ar$), 7.75 (8H, *s*, ArH), 10.14 (4H, *s*, OH); *Found*: C, 79.29; H, 9.82. *Calcd.* for $C_{76}H_{112}O_8$: C, 79.12; H, 9.79%.

(b) *p-Dodecylcalix[4]arene*. *p*-Dodecanoylcalix[4]arene (3.1 g, 2.7 mmol) was dissolved in a mixture of trifluoroacetic acid (140 mL) and carbon tetrachloride (70 mL) and the solution was stirred for 10 min at room temperature. Triethylsilane (6.2 g, 55 mmol) was added dropwise to this solution and the resultant solution was stirred at room temperature for 137 h. The solution was concentrated *in vacuo*. The residue was dissolved in carbon tetrachloride to remove residual CF_3COOH and the solvent was concentrated to give a crude product, which was dissolved in chloroform, treated with *ca.* 5% $NaHCO_3$ solution and was washed with water for neutralization. After being dried over sodium sulfate, the chloroform solution was concentrated. The resultant crude product was recrystallized from benzene–ethanol to give *p*-dodecylcalix[4]arene as a pale brown powder (1.8 g, 59%); m.p. 104–105°C; ν_{max} (KBr)/cm^{-1} 2963 (OH), 1481, 1186; δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 0.88 [12H, *br t*, $CH_2CH_2(CH_2)_9CH_3$], 1.26 [36H, *s*, $CH_2CH_2(CH_2)_9CH_3$], 1.60 [8H, *br m*, $CH_2CH_2(CH_2)_9CH_3$], 2.39 [8H, *br t*, $CH_2CH_2(CH_2)_9CH_3$], 3.76 (8H, *br s*, ArCHAr), 4.10 (8H, *s*, ArCHAr), 6.82 (8H, *s*, ArH), 10.17 (4H, *s*, OH); *Found*: C, 83.38; H, 11.11. *Calcd.* for $C_{76}H_{120}O_4$: C, 83.15; H, 11.02%.

(c) *Cone-3(4Es)*. *p*-Dodecylcalix[4]arene (0.5 g, 0.46 mmol), ethyl bromoacetate (0.51 g, 18 mmol) and potassium carbonate (2.5 g, 18 mmol) were dissolved in acetone (80 mL) containing a drop of DMF. The mixture was refluxed for 16 h. After cooling, the solution was poured into carbon dioxide-saturated water (200 mL). The resultant white precipitate was collected and recrystallized from methanol–chloroform three times to give 25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]-*p*-dodecylcalix-[4]arene with a cone conformation, cone-**3**(4Es) as white crystals (0.47 g, 39%); m.p. 49–50°C; ν_{max} (KBr)/cm^{-1} 2924 (CH, each), 1763, 1741 (C=O), 1466 (Ar); δ_H (90 MHz, $CDCl_3$, 25°C, TMS) 0.88 [12H, *br t*, $CH_2CH_2(CH_2)_9CH_3$], 1.26 [48H, *m*, $CH_2CH_2(CH_2)_9CH_3$ and OCH_2CH_3], 1.60 [8H, *br*, $CH_2CH_2(CH_2)_9CH_3$], 2.26 [8H, *br t*, $CH_2CH_2(CH_2)_9CH_3$], 3.17 (4H, H_{AB}, *J* 14, ArCHAr), 4.26 (8H, *q*, *J* 7, OCH_2CH_3), 4.19 (4H, H_{AB}, *J* 14, ArCHAr), 4.71 (8H, *s*, OCH_2CO), 6.44 (8H, *s*, ArH); *Found*: C, 72.09; H, 12.22. *Calcd.* for $C_{72}H_{144}O_{12}$: C, 71.95; H, 12.08%.

2.1.11. *Synthesis of Other Compounds*

25,27-Dimethoxy-26,28-dihydroxy-*p*-t-butylcalix[4]arene **1**(2Me2OH) [19], 25,26,-27, 28-tetrakis(ethoxyethoxy)-*p*-t-butylcalix[4]arene Cone-**1**(4EtOEt) [26], 25,27-bis[(ethoxycarbonyl)methoxy]-26,28-bis(2-pyridylmethyl)-*p*-t-butylcalix[4]arene **1**(2Py2Es) [22], 25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]-*p*-t-butylcalix[4]-arene **1**(4Es) [27], 25,26,27,28-tetramethoxy-*p*-t-butylcalix[4]arene **1**(4Me) [28] and 25,26,27,28-tetrapropoxy-*p*-t-butylcalix[4]arene Cone-**1**(4Pr) [28]: These compounds were prepared in a manner similar to that described previously.

2.2. PREPARATION OF ION-SLECTIVE ELECTRODES

A typical method for the preparation of ion-selective electrodes is as follows: poly(vinylchloride) (PVC: $p = 1100$, 50 mg), plasticizer (2-fluorophenyl-2′-nitrophenyl ether (**10**, 100 mg) unless otherwise mentioned), *p*-tetrakis(chlorophenyl)borate potassium salt (1 mg; as an additive) and ligand (**1–3**, 5 mg, unless otherwise mentioned) were dissolved in tetrahydrofuran (THF, 2 mL). The solution was poured into a flat Petri dish (diameter 3 cm). The dish was kept in a calcium chloride vessel to protect the sample from humidity. The whole system was covered by a box and the solvent was slowly evaporated at room temperature. This treatment gave a transparent and elastic membrane: the thickness was 0.15–0.20 mm. A piece of the membrane was cut out and attached to one side of a PVC tube (outer diameter 8 mm; inner diameter 4 mm and height 7 cm) by an adhesive composed of the former solution which does not contain the ligand and the additive. After *ca.* 30 min, the tube was filled with 10^{-3} mol dm^{-3} of sodium chloride solution and the Ag/AgCl (5 cm × 3 mm) plate was inserted. This was used as a working electrode.

2.3. MEASUREMENTS OF MEMBRANE POTENTIALS

The working electrode and one end of an elastic PVC tube filled with 0.5 w/w% agar [which was dissolved in lithium acetate (10^{-1} mol dm^{-3}) solution (salt bridge)] were immersed in a sample solution. The other end of the salt bridge and a reference electrode (Ag/AgCl) were dipped in a saturated KCl solution. Both electrodes were connected to an electrometer (Advantest Co. R-8240). The whole system described above is summarized as follows; Ag/AgCl|aq. NaCl (10^{-3} mol dm^{-3})|membrane|sample solution|aq. lithium acetate (10^{-1} mol dm^{-3})|KCl (saturated)|Ag/AgCl. All the measurements were performed by SSM at 25°C. In general, the response speed of the electrodes was excellent: it took only 5–10 s to reach the stationary voltage. In some cases the drift was observed after the stationary state was reached. However, the range was negligibly small in comparison to the stationary voltage, so we consistently adopted the initial stationary voltage. Selectivity coefficients were calculated by the Nicolsky–Eisenman equation from the data at 10^{-1} mol dm^{-3} unless otherwise mentioned.

$$\log K^{\text{pot}}_{\text{Na,M}} = Z_{\text{Na}}F(E_{\text{M}} - E_{\text{Na}})/2.3RT - (Z_{\text{Na}}/Z_{\text{M}}) \log a_{\text{M}} + \log a_{\text{Na}}$$

where a_{Na} and a_{M} are the activities of Na^+ and other cations, respectively, calculated by the Debey–Hückel equation.

2.4. CALCULATION OF POINT CHARGES

A semiempirical molecular orbital calculation (MNDO-PM3) was carried out for the phenol derivatives. Input structures of these compounds were established by the combination of the standard bond lengths [20]. Molecular structures were optimized by MOPAC ver. 6.0 [21] using PM3 Hamiltonian under the condition that the plane composed of two ligand oxygens is perpendicular to the benzene ring. These calculations were performed on the engineering workstation system: SUN 4/2 and IRIS 4D 35G.

3. Results and Discussion

3.1. INFLUENCE OF CONFORMATIONS ON THE ION SELECTIVITY

We have found that conformational isomers of ionophoric calix[4]arenes can be synthesized by using metal template effects [22–24]. It was shown on the basis of two-phase solvent extraction that the cone conformer shows Na^+ selectivity whereas the other three conformers, with one or two invested phenyl units, show K^+ selectivity [22, 24]. The change in the ion selectivity was explained on the basis of the X-ray crystallographic data: in the conformers with invested phenyl units the phenyl groups constructing an ionophoric cavity are more or less parallel to each other, resulting in a cavity larger than that in the Na^+-selective cone conformer [22, 25]. In Figure 1 the ion selectivities against Na^+ as a standard ($\log K^{pot}_{Na,M}$) are plotted against ionic diameters. As is already known, cone-**1**(4Es) shows the remarkably high selectivity towards Na^+: in the present system, $\log K^{pot}_{Na,M} = -3.4$ for Li^+, -2.6 for K^+, -3.8 for Rb^+, -4.3 for Cs^+ and -4.8 for

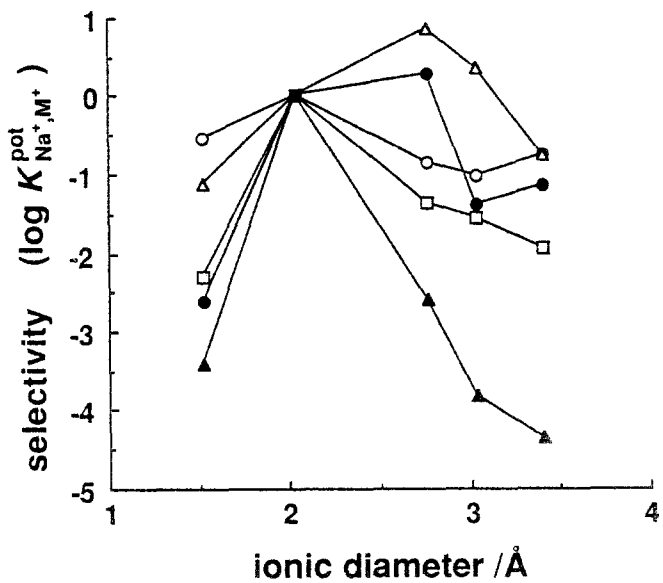


Fig. 1. Na^+ selectivity of conformational isomers: **10** was used as plasticizer; cone-**1**(4Es) (▲), cone-**1**(2Py2Es) (□), *p*-cone-**1**(4Es) (●), *p*-cone-**1**(2Py2Es) (○), 1,3-alternate-**1**(2Py2Es) (△).

NH_4^+. Cone-**1**(2Es2Py), the ionophoric cavity of which is composed of two esters and two pyridines [22, 24], also shows Na^+ selectivity: $\log K^{pot}_{Na,M} = -2.3$ for Li^+, -1.4 for K^+, -1.6 for Rb^+, -1.9 for Cs^+ and -1.6 for NH_4^+. The results indicate that the Na^+ selectivity observed for cone-**1**(2Es2Py) is not so sharp as that observed for cone-**1**(4Es). Examination of CPK molecular models indicates that the ionophoric cavity in cone-**1**(2Es2Py) is sterically crowded: for example, when two pyridine nitrogens interact with a bound Na^+ ion, 6-H protons in the distal pyridine nuclei undergo steric repulsion. We consider, therefore, that cone-**1**(4Es) can compose an ionophoric cavity from four esters without inducing such steric repulsion. It is also seen from Figure 1 that partial-cone-**1**(4Es) [23] shows the K^+ selectivity, although the selectivity against Na^+ is not so large ($\log K^{pot}_{Na,M} = 0.27$). As mentioned above, the K^+ selectivity is expected from the X-ray crystallographic studies and two-phase solvent extraction [23, 30]. On the other hand, partial-cone-**1**(2Es2Py), in which one benzene ring connected to the acetate ester is reversed, showed Na^+ selectivity regardless of the K^+ selectivity in two-phase solvent extraction [22]. This discrepancy is not well understood. It has been established that in 1,3-alternate-**1**(2Es2Py) the two ester groups, but not the two pyridine groups, act as a primary metal binding site [22]. Since the four phenyl rings are parallel to each other [37], the distance between two ester groups are significantly longer than that between two distal ester groups in cone-**1**(4Es). Thus, the ionophoric cavity constructed on 1,3-alternate-**1**(2Es2Py) is larger than that constructed on cone-**1**(4Es). This is why 1,3-alternate-**1**(2Es2Py) shows the clear K^+ selectivity. The foregoing results indicate that the metal selectivity of ionophoric calix[4]arenes in the electrode system can be conveniently changed by the conformational change.

3.2. CARBONYL OXYGEN VS. ETHEREAL OXYGEN IN THE LIGAND GROUP

As demonstrated above, cone-**1**(4Es) shows excellent Na^+ selectivity. However, the ligand groups used therein are esters which are not so stable in acidic or basic pH regions. In fact, we previously found that cone-**1**(4Es) is partially hydrolyzed during two-phase solvent extraction [31]. Once an ester group is incorporated into a ligand, it would be impossible to modify it any more. We considered that this defect may be remedied by the replacement of the esters with the ethers. With this objective in mind we used cone-**1**(4EtOEt) as an ionophore for the ion-selective electrode. Although cone-**1**(4EtOEt) was Na^+-selective, the selectivity against other alkali metal cations was rather disappointing (Figure 2); $\log K^{pot}_{Na,M} = -2.0$ for Li^+, -0.4 for K^+, -1.2 for Rb^+, -1.6 for Cs^+ and -1.6 for NH_4^+. The result is attributed to the rotational freedom of the flexible—$CH_2CH_2OCH_2CH_3$ chains composing a metal binding site.

We considered that to remove the defect of cone-**1**(4EtOEt) one should suppress the rotation of the ligand groups. We thus introduced furan rings instead of simple ether chains. Examination of a CPK molecular model for cone-**1**(4Fu) revealed that the ionophoric cavity composed of four furan rings is relatively crowded and the rotation of each furan ring is sterically restricted. In the synthesis of cone-**1**(4Fu) we noticed that the product contains six isomers due to the chirality at 1-C in the furan ring; they are *RRRR*, *SSSS*, *RRSS*, *RSRS*, *SSRS* and *RRSR*. We thus isolated a

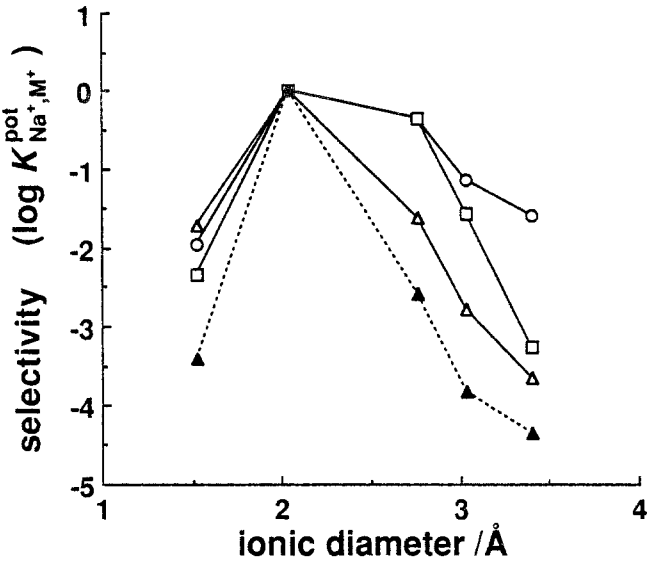


Fig. 2. Comparison of the ester ligand with the ether ligand: **11** was used as plasticizer; cone-**1**(4EtOEt) (○), cone-**1**(4Fu) (□), cone-**1**(2Fu2Es) (△), cone-**1**(4Es) (▲).

racemic mixture of *RRRR* and *SSSS* by HPLC, which is expected to have the most organised ionophoric cavity. The NMR spectrum of the isolated compound showed a single peak each for benzene rings and t-butyl groups and an H_{AB} pattern for methylene bridges. These results suggest that the resultant compound is the mixture of *SSSS* and *RRRR* with high molecular symmetry. As shown in Figure 2, the ion selectivity is improved in comparison to cone-**1**(4EtOEt), indicating that the suppression of the rotational freedom is an important factor in the design of calixarene-based ionophores for the electrode: $\log K^{pot}_{Na,M} = -2.6$ for Li^+, -0.4 for K^+, -1.6 for Rb^+, -3.3 for Cs^+ and -2.3 for NH_4^+.

We also synthesized cone-**1**(2Es2Fu) which has two esters and two furans with the *RS* configuration about 1-C in the furan rings. The NMR spectrum of the resultant compound showed a complicated pattern for methylene bridges which is clearly different from that for the *RR* and *SS* mixture that should give the single H_{AB} pattern. This indicates that the product has the *RS* configuration. This is further supported by the facts that the compound has a sharp m.p. (205–206°C) and gives a single HPLC peak. As shown in Figure 2, the Na^+ selectivity is further improved but still inferior to that for cone-**1**(4Es). Then, what is the origin of the remarkably high Na^+ selectivity for cone-**1**(4Es)? We estimated the point charges of oxygen atoms in each phenol unit by MOPAC. We here assumed the conformation in which the plane composed of two ligand oxygens ($OCH_2C{=}O$ or OCH_2CHO) is perpendicular to the benzene ring (Figure 3). The point charges of the ethereal oxygens in 1-phenoxymethylfuran are -0.180 to -0.246 esu, whereas the carbonyl oxygen in ethyl phenoxyacetate shows a much higher point charge (-0.350 esu). It is known that 25,26,27,28-tetramethoxycalix[4]arene derivatives show a selectivity towards Li^+ rather than towards Na^+ [34]. This implies that the Na^+ selectivity observed for cone-**1**(4Es) is primarily associated with the carbonyl

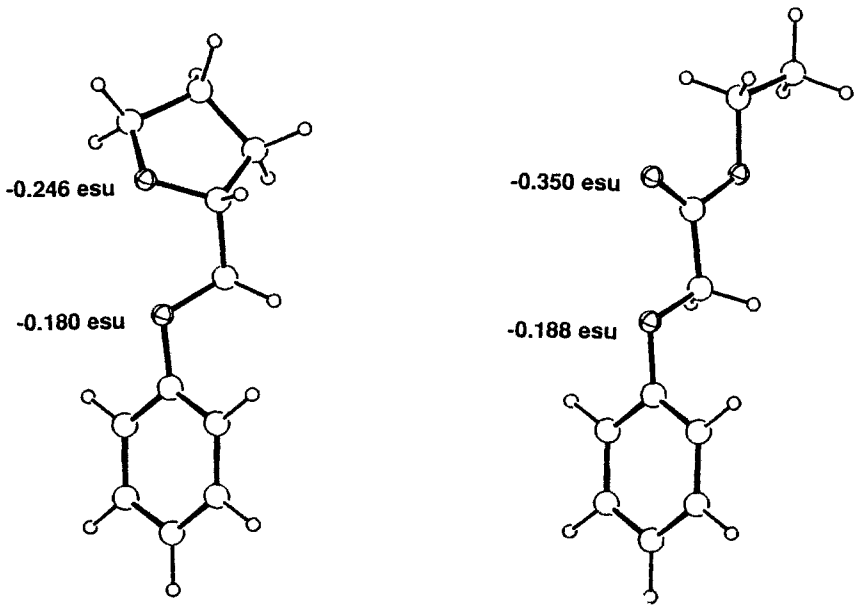


Fig. 3. ORTEP view [37] for optimized structures calculated by MOPAC.

oxygens, although the ethereal oxygens contribute to the Na^+-binding to some extent. One can thus conclude that the high Na^+ selectivity stems from the high point charge of the four carbonyl oxygens which are arranged to suit the size of the Na^+ ion. This electrostatic situation is the first advantage of cone-**1**(4Es). It is known that in ^1H NMR spectroscopy $\Delta\delta$ between H_{exo} and H_{endo} in the $ArCH_2Ar$ methylene protons of calix[4]arenes serves as a measure of the 'flattening'; $\Delta\delta$ is generally 0.9 ppm for a system in the cone conformation and in the 'flattened' conformation $\Delta\delta$ is significantly decreased [35]. We have found that $\Delta\delta$ for vacant cone-**1**(4Es) is 1.80 ppm, indicating that the phenol units are more parallel because of steric crowding among the ester groups wheras it is decreased to 0.98 ppm upon binding to Na^+ [36]. This implies that the four phenol units must experience the 'flattening' for the $-OCH_2CO-$ groups to coordinate to the central Na^+ ion. Very fortunately, the $-C-C(=O)-O-$ linkage adopts a planar structure because of the sp^2 nature of the carbonyl carbon and steric repulsion among the ligand groups scarcely takes place. On the other hand, the 'flattening' of the furan rings accompanies considerable steric crowding on the narrow lower rim. This causes the disadvantage in the constitution of a neat ionophoric cavity.

We consider that because of the above-mentioned electrostatic and steric advantages, cone-**1**(4Es) can exhibit the remarkably high Na^+ selectivity.

3.3. MODIFICATION OF THE SUBSTITUENTS ON THE UPPER RIM

As described above, an ionophoric cavity constructed on the lower rim with the ethoxycarbonylmethyl group already shows high Na^+ selectivity. It thus

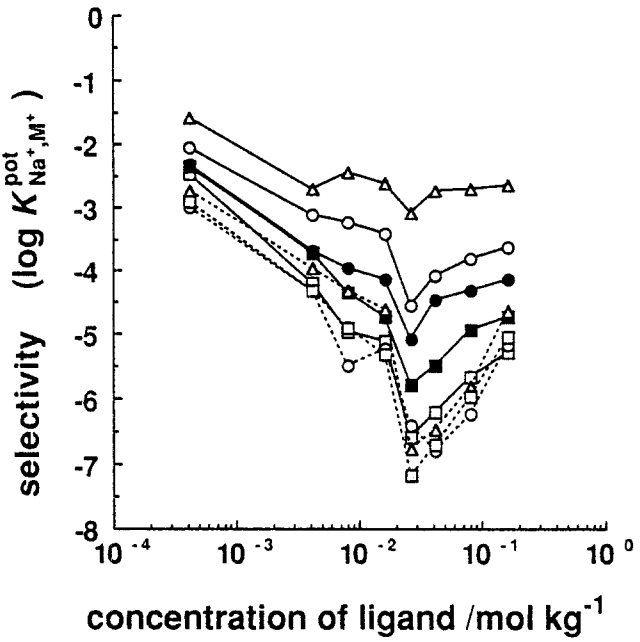


Fig. 4. Na^+ selectivity of cone-**3**(4Es) in membrane; Li^+ (—○—), K^+ (—△—), NH_4^+ (—□—), Rb^+ (—●—), Cs^+ (—■—), Mg^{2+} (--○--), Ca^{2+} (--△--) and Ba^{2+} (--□--).

occurred to us that the ion selectivity in the electrode system may be enhanced by the modification of the substituents on the upper rim rather than by the modification of the ligand groups on the lower rim. We thus introduced long aliphatic chains into the *para*-positions. In particular, we decided to employ the *t*-octyl group because we previously experienced that this group is capable of efficiently enhancing the solubility of calixarenes in organic solvents. Cone-**1**(4Es) is insoluble in methanol and very poorly soluble in hexane. Cone-**2**(4Es) with *n*-dodecyl groups at the *para*-positions is moderately soluble in hexane and cone-**3**(4Es) with *t*-octyl groups at the *para*-positions is soluble in almost all organic solvents except methanol. The results suggest that cone-**3**(4Es) would be homogeneously dissolved in the plasticizer through the solvation by plasticizer molecules.

As shown in Figure 5, the Na^+ selectivity for cone-**2**(4Es) is generally superior to that for cone-**1**(4Es). Both electrodes showed near Nernstean slope; 57–62 mV between the range from 10^{-1} to 10^{-5}. Moreover, the PVC-**10**-cone-**3**(4Es) membrane showed an ordinary Nernst response down to 10^{-6} mol dm^{-3} (Figure 6). Excitingly, the Na^+ selectivity was superior to that for cone-**1**(4Es) (Figure 4): $\log K^{pot}_{Na,M} = -4.6$ for Li^+, -3.1 for K^+, -5.1 for Rb^+, -5.8 for Cs^+ and -6.6 for NH_4^+. It is worthwhile to mention that $\log K^{pot}_{Na,M} = -4.6$ even at $[Mg^{2+}] = 10^{-6}$ mol dm^{-3}. These values are even superior to those for bis(12-crown-4)dodecylmethylmalonate which is known to possess the highest Na^+ selectivity among crown ether compounds [32, 33].

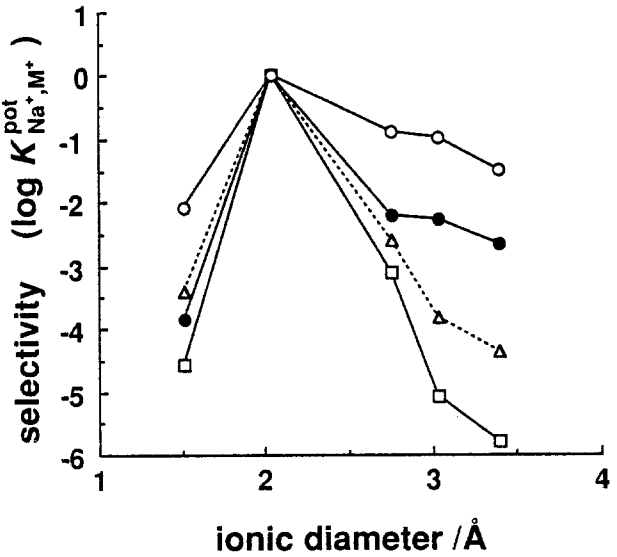


Fig. 5. Na^+ selectivity of cone-**1**(4Es)-**11** (--△--), cone-**2**(4Es)-**11** (—○—), cone-**3**(4Es)-**11** (—□—) and bis[(12-crown-4)methyl]methyldodecylmalonate-**10** (—●—).

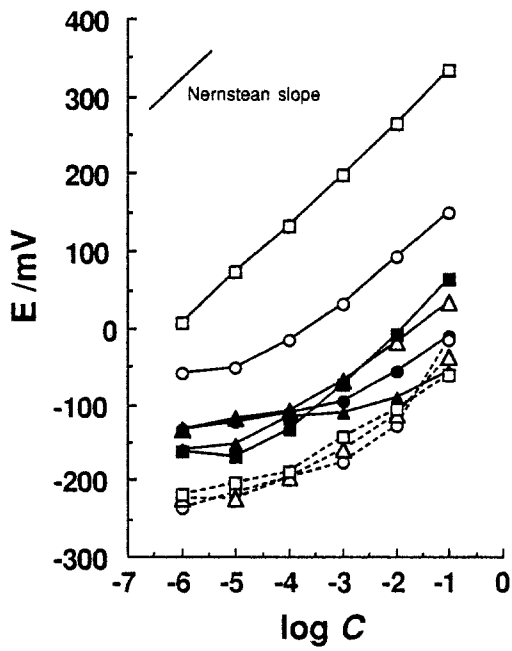


Fig. 6. Calibration plots for concentration of various ions; Li^+ (—■—), Na^+ (—□—), K^+ (—○—), NH_4^+ (—▲—), Rb^+ (—△—), Cs^+ (—●—), Mg^{2+} (--○--), Ca^{2+} (--△--) and Ba^{2+} (--□--).

Table I. Selectivity dependence of cone-**3**(4Es) on plasticizers

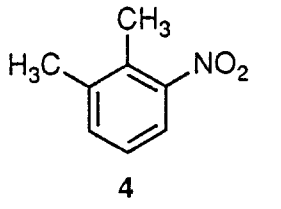
Plasticizer	Selectivity log $K^{pot}_{Na+,M+}$								
	Li^+	Na^+	K^+	Rb^+	Cs^+	NH_4^+	Mg^{2+}	Ca^{2+}	Ba^{2+}
4	−4.1	0	−2.8	−4.5	−5.5	−6.1	−6.1	−5.6	−6.1
5	−3.6	0	−2.7	−4.1	−4.3	−5.2	−6.7	−5.9	−6.2
6	−2.8	0	−2.1	−3.5	−4.2	−4.6	−4.9	−4.0	−4.9
6[a)]	−3.4	0	−2.4	−3.8	−4.6	−4.8	−5.6	−4.8	−5.4
7	−2.1	0	−1.5	−2.9	−3.6	−4.0	−4.7	−4.5	−4.9
7[a)]	−3.0	0	−1.9	−3.4	−4.1	−4.5	−5.4	−5.2	−6.1
8	−3.6	0	−2.6	−4.4	−5.3	−5.7	**−7.0**	−6.3	−6.7
9	−4.0	0	−2.8	−4.7	−5.3	−6.3	−6.9	−6.6	−6.7
10	**−4.6**	0	**−3.1**	**−5.1**	−5.8	**−6.6**	−6.3	**−6.7**	**−7.1**
11	−2.4	0	−1.7	−3.4	−4.7	−4.7	−6.5	−6.1	−6.5
12	−3.6	0	−2.7	−4.4	−5.9	−5.9	−6.9	−6.5	−6.7
13	−3.4	0	−2.6	−4.3	−5.7	−5.8	−6.6	−6.0	−6.4
14	−3.7	0	−2.7	−4.5	**−6.1**	−6.0	−7.0	−6.5	−7.0
15	−3.4	0	−2.4	−4.1	−5.6	−5.4	−5.9	−5.3	−5.8
16	−1.7	0	−2.5	−3.5	−3.6	−2.3	−4.5	−4.2	−4.5

[a)]Data at 10^{-2} adopted.

We prepared the cone-**3**(4Es) containing PVC membranes with 13 plasticizers and determined the log $K^{pot}_{Na,M}$ values (Table I). All the membranes showed near Nernstean slope (at least 53 mV/decade) to the region of 10^{-4}, except plasticizers **6** and **7**. In the case of those two plasticizers, the sensitivity in the region of 10^{-2} to 10^{-1} proved to be quite low. This phenomenon is not well understood. In this case the selectivity value increases when 10^{-2} data were adopted. The highest log $K^{pot}_{Na,M}$ value (−3.1) was observed for 2-fluorophenyl-2′-nitrophenyl ether (**10**) as a plasticizer. Plasticizer **10** resulted in the excellent log $K^{pot}_{Na,M}$ values for other competing metal cations and the highest values are attained not only for K^+ but also Rb^+, NH_4^+, Ca^{2+} and Ba^{2+}. The highest log $K^{pot}_{Na,M}$ values for Cs^+ and Mg^{2+} were obtained in the presence of *o*-nitrophenyl dodecyl ether (**14**) and DOS (**8**), respectively.

3.4. CALIX[4]ARENES WITH DEFECTIVE IONOPHORIC CAVITIES

As summarized in Table II, lower-substituted calix[4]arenes [e.g. **1**(2Fu2OH), **1**(2Me2OH), and **1**(2MeOMe2OH)] showed the selectivity order of $Cs^+ > Rb^+ > K^+ > Na^+ > Li^+$. This order is in line with the hydrophobicity order of these alkali metal cations. There is no precedent for the selective binding of Cs^+ to calix[4]arene derivatives, so that it is inconceivable that these calix[4]arenes provide an ionophoric cavity large enough to bind Cs^+. We thus consider that the response is ascribed to the interaction of hydrophobic cations onto the electrode surface. Presumably, the metal-binding ability of two Fu groups in **1**(2Fu2OH) or two MeOMe groups in **1**(2MeOMe2OH) is suppressed to some extent by intramolecular hydrogen-bonding interactions with unsubstitued OH groups.



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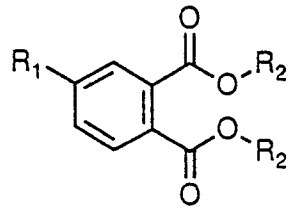
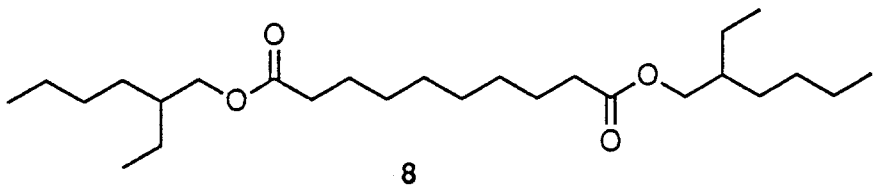


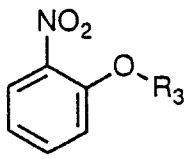
5 R_1=H, R_2=ethylhexyl

6 R_1=NO_2, R_2=ethylhexyl

7 R_1=NO_2, R_2=*n*-octyl



8



9 R_3=phenyl

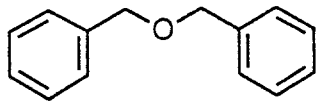
10 R_3=2-fluorophenyl

11 R_3=*n*-octyl

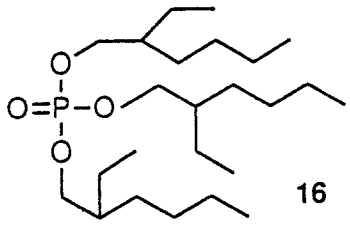
12 R_3=*n*-nonyl

13 R_3=*n*-decyl

14 R_3=*n*-dodecyl



15



16

As mentioned above, we have confirmed that **1**(4Me) is capable of binding Li^+ or Na^+ in aprotic solvents [34]. In two-phase solvent extraction (water–dichlormethane), however, this calix[4]arene could not extract any alkali picrates. This implies that the ionophoricity of **1**(4Me) is not strong enough so as to overcome the hydration energy. As recorded in Table II, neither **1**(4Me) nor **1**(4Pr) showed selectivity towards Li^+ or Na^+. This indicates that the ionophoric properties of these calix[4]arenes appear only in aprotic solvents where metal cations are less solvated.

The comparison of the ion selectivity for **1**(4EtOEt) and **1**(4EtOPr) ($Na^+ > K^+ > Rb^+ > Cs^+ > Li^+$) with that for **1**(4MeOMe) ($Cs^+ > Rb^+ > K^+ > Na^+ > Li^+$) reveals that the effective ligand structure is —O—C—C—O— rather than —O—C—O—. Strangely, **1**(4EtOPh) showed the simple hydrophobicity order, even though it has four —O—C—C—O— ligand groups. Examination of CPK molecular models suggests that, as already observed for **1**(4Es) [36], the four phenoxyethoxy groups must be flattened for the oxygen atoms to coordinate to a bound metal cation. Before the oxygen atoms reach the metal cation, the phenyl groups undergo steric repulsion. The finding indicates that to design a neat

Table II. Selectivity dependence on defective ligands

Ligand	Plasticizer	Selectivity $\log K^{pot}_{Na^+,M^+}$					
		Li^+	Na^+	K^+	Rb^+	Cs^+	NH_4^+
1(4EtOEt)	**10**	−1.6	0	−0.4	−1.2	−1.6	−1.6
1(4EtOPr)	**10**	−1.8	0	−0.2	−0.9	−0.9	−1.3
1(4EtOPh)	**10**	−1.1	0	1.0	1.5	2.3	0.3
1(2Me2Am)	**10**	−1.5	0	−0.1	−0.3	−1.5	−0.2
1(2Me2Es)	**11**	0.0	0	0.9	1.5	2.8	0.8
1(2Fu2OH)	**11**	−0.6	0	0.5	0.6	1.3	0.3
1(4Fu)	**11**	−2.6	0	−0.4	−1.6	−3.3	−2.3
1(4Fu)[a)]	**11**	−1.7	0	0.3	−0.1	−0.6	−0.6
1(2Me2OH)	**10**	−0.9	0	1.2	1.8	2.7	0.9
1(2MeOMe2OH)	**10**	−0.4	0	1.9	2.6	3.3	1.4
1(4MeOMe)	**11**	−1.5	0	0.4	1.0	1.9	0.0
1(4Me)	**10**	−0.6	0	1.1	1.3	1.7	0.6
1(4Pr)	**10**	−1.3	0	0.1	0.4	1.2	−0.2
none	**10**	−0.2	0	1.6	2.1	2.6	1.0
none	**11**	−0.4	0	2.0	2.6	3.3	1.4

[a)] **1**(4Fu)′ contains stereoisomers other than *R,R,R,R*- or *S,S,S,S*-isomers.

ionophoric cavity, a bulky substituent is not recommended for R in the —O—C—C—O—R groups.

4. Conclusion

The purpose of the present study was to obtain insights into a relationship between the calix[4]arene structure and the ion selectivity (particularly, Na^+ selectivity) in the electrode system. In order to modify the ionophoric cavity on the lower rim we introduced several ligand groups, but we could not discover any ligand group better than the ethoxycarbonylmethyl group. This group consists of a strongly negatively polarized carbonyl oxygen and a sterically less bulky sp^2-carbon. The characteristics are thus advantageous for metal binding, not only from an electrostatic viewpoint but also from a steric viewpoint. On the other hand, the ion selectivity was efficiently improved by the modification of the alkyl group on the upper rim. The t-octyl group, which is capable of enhancing the miscibility of calixarenes with organic solvents, was particularly effective. It seems to us that these findings provide a potential strategy for the design of highly ion-selective electrodes: the core must have a rigid metal-binding cavity, while the branch must have flexible, solvophilic chains. We are now trying to extend this concept to the molecular design of new Li^+-selective and K^+-selective electrodes.

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