Calix[4]arene derived tetraester receptors modified at their wide rim by polymerizable groups

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The synthesis of calix[4]arene tetraester ionophores containing polymerizable groups at their wider rim is reported. Calixarene monomers with one or two methacrylamide groups were copolymerized with methyl methacrylate, yielding linear polymers with pendant calixarene groups or crosslinked polymers. Extraction studies with the soluble copolymers and with the corresponding pivalamides as model compounds showed no difference in the extraction ability and selectivity. Potentiometric measurements of membrane electrodes prepared with the polymeric calixarene ionophores indicated that the high selectivity, the slope of the response curve and the low detection limit of membranes containing non-bonded calixarene ionophores are retained while the lifetime of the polymeric membranes is increased.

The design of improved ion-sensing materials has attracted much attention from chemists in recent years. Calix[4]-arenes—macrocyclic phenol–formaldehyde tetramers—are easily synthesized and functionalized not only at their narrow rim (by derivatization of the phenolic OH groups), but also at their wide rim (by substitution of the para positions of the phenolic rings).[1] Owing to their well-defined three-dimensional structure they are universal starting materials for the preparation of synthetic ionophores by the attachment of various receptor groups.

Membrane techniques are particularly suitable for a rapid screening of the selectivities of different ligands towards inorganic ions or organic species. Most ion-selective membranes consist of a polymeric support containing the low molecular weight ion-selective receptor molecules and other membrane components (*e.g.*, plasticizer, lipophilic anionic additives). Leaching of these low molecular weight compounds out of the membrane leads to severe deterioration of the sensor response. To overcome this problem covalent attachment of the receptor molecules to a polymer backbone is proposed.

In recent years various attempts have been undertaken to incorporate calixarenes into different polymers[2–7] including self-assembled systems.[7] There are two general strategies to prepare covalently linked calixarene-based polymers: attachment of the calixarene by reaction with a suitably functionalized polymer or oligomer[4,6,8] or preparation of a calixarene monomer and its polymerization[9] or copolycondensation[4,10] with typical monomers. The latter way gives more defined products since there is no risk of incomplete substitution of the functionalized polymer. Thus, calixarene monomers have been incorporated into polymer backbones utilizing functional groups at the narrow[10] as well as at the wide rim.[4,11] Recently, Blanda and Adou have obtained linear calixarene-based polymers with pendant calixarene systems by copolymerization of monovinyl calixarene derivatives with typical vinyl monomers.[11]

Calixarenes substituted by four ethoxycarbonylmethoxy groups at the narrow rim are well-known sodium selective ionophores.[12] Since now, all attempts to immobilize this type of ligand on a polymer matrix were performed *via* the modification of the narrow rim of the calixarene macrocycle,[9,13] usually starting with the selective mono hydrolysis of one ester function.[14] The main disadvantages of this approach are a potential distortion of the receptor region (binding site) by the linkage to the polymer chain and interaction of the polymer backbone with the receptor groups, which can disturb the complexation selectivity. However, in special cases the insertion of ionophoric calixarene units into a polymer chain may give materials where the intrinsic properties of the macrocycle are enhanced by conjugation with the polymer backbone.[2]

Since the complexation of a cation in tetraester derivatives takes place at the narrow rim it seems advantageous to use the other rim of the macrocycle for the introduction of a polymerizable group (compare Fig. 1). In this study we describe the synthesis of new methacrylamide derivatives of calix[4]arene bearing the polymerizable group at the wide rim of the calix[4]arene, while all OH groups of the narrow rim

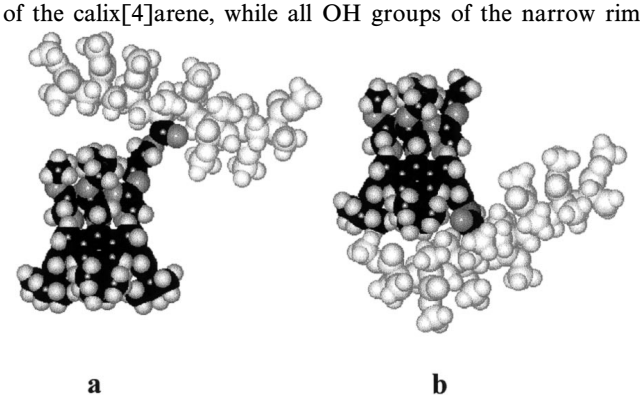


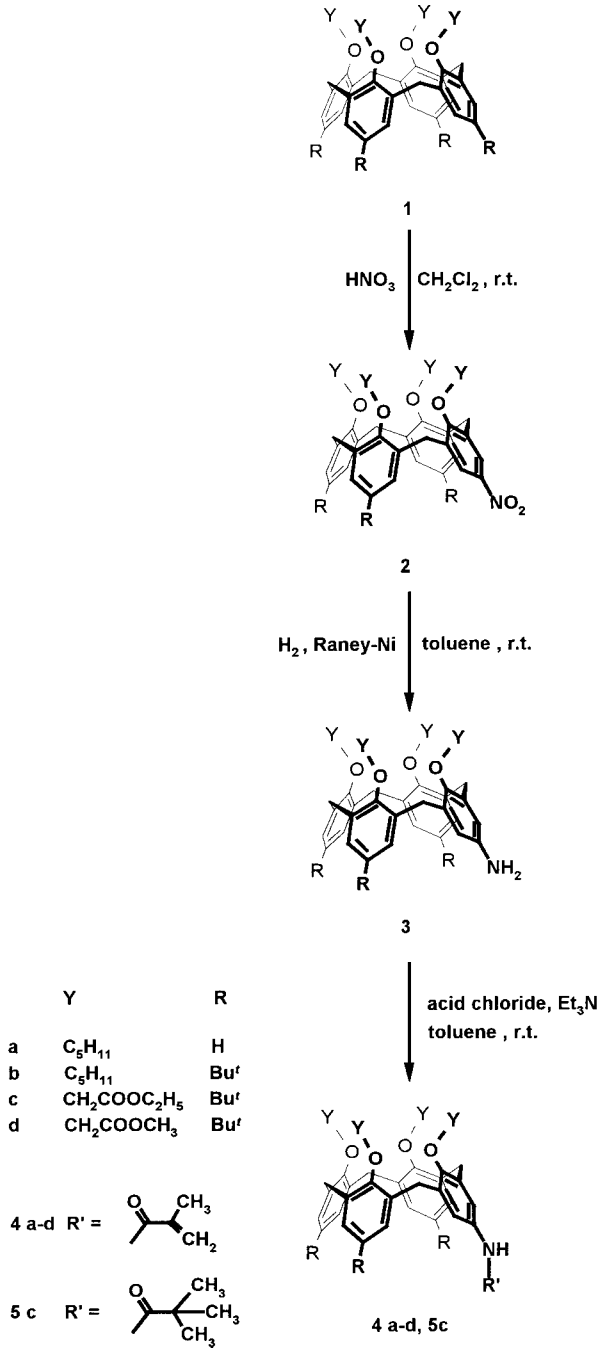
Fig. 1 Illustration of a polymer bound calix[4]arene tetraester molecule attached (*a*) at the narrow rim *via* O–CH_2–COO–CH_2CH_2–OOC-groups and (*b*) at the wide rim *via* NH–CO–C-groups. The tetraester binding site is not influenced by the polymer chain in the latter case.

may be converted into a symmetrical binding site. The copolymerization of these monomers with methyl methacrylate was studied and the properties of the polymeric calixarene receptors, especially the complexing properties, were investigated in comparison to systems based on the low molecular weight analogs.

Results and discussion

Syntheses of monomeric and model compounds

The preparation of calixarene monomers with one polymerizable group at the wide rim is presented in Scheme 1. Calixarene tetraethers **1** in the cone conformation were used as starting materials. ipso-Nitration of **1b–d** was successfully applied for the introduction of only one nitro group to the wide rim of the macrocycle. The reaction conditions (dichloromethane as main solvent, concentrated nitric acid, room temperature),[15] which are slightly different for the different compounds, can be used also for the mononitration of **1a**.



Scheme 1

Subsequent reduction of the nitro group of **2** by catalytic hydrogenation (Raney-Ni, r.t., normal pressure) yields amino derivatives **3**, which can be used for the further steps, usually without additional purification.

The final monomers **4a–d** and model compound **5** were obtained with yields of more than 90% by acylation with methacryloyl or pivaloyl chlorides in dry toluene or THF in the presence of triethylamine. The ^{1}H NMR spectrum of the final calixarene monomers show signals characteristic for the methacrylamide group; for example, for **4c** the NH proton is at 6.69 ppm, the C=CH_2 protons at 5.46 and 5.23 ppm and the CH_3 protons 1.84 ppm. The model compound **5c** shows instead a NH proton 6.57 ppm and singlet for the *tert*-butyl group. Two pairs of doublets for the two different Ar–CH_2–Ar groups and two singlets (ratio 2 : 1) for the Ar–$C(CH_3)_3$ groups are found for all compounds **4** and **5**. In contrast to the mononitro compounds **2c**, **d**, the diastereotopic protons of two O–CH_2–CO groups are not indicated by a pair of doublets in compounds **4c**, **d** and **5**.

Calixarene derivatives having two methacrylamide groups at the wide rim can be synthesized in a similar way. Starting with diether **6** (Scheme 2) ipso-nitration can be used to substitute selectively the two (more activated) phenolic units.[16] Subsequent etherification of **7**, assisted by the template effect of K^+ cations, allows one to obtain the tetraether **8** exclusively in the cone conformation. The reduction of the nitro groups followed by acylation as described above leads finally to the dimethacrylamide **10** and the dipivalamide **11** in yields of 95 and 73%, respectively.

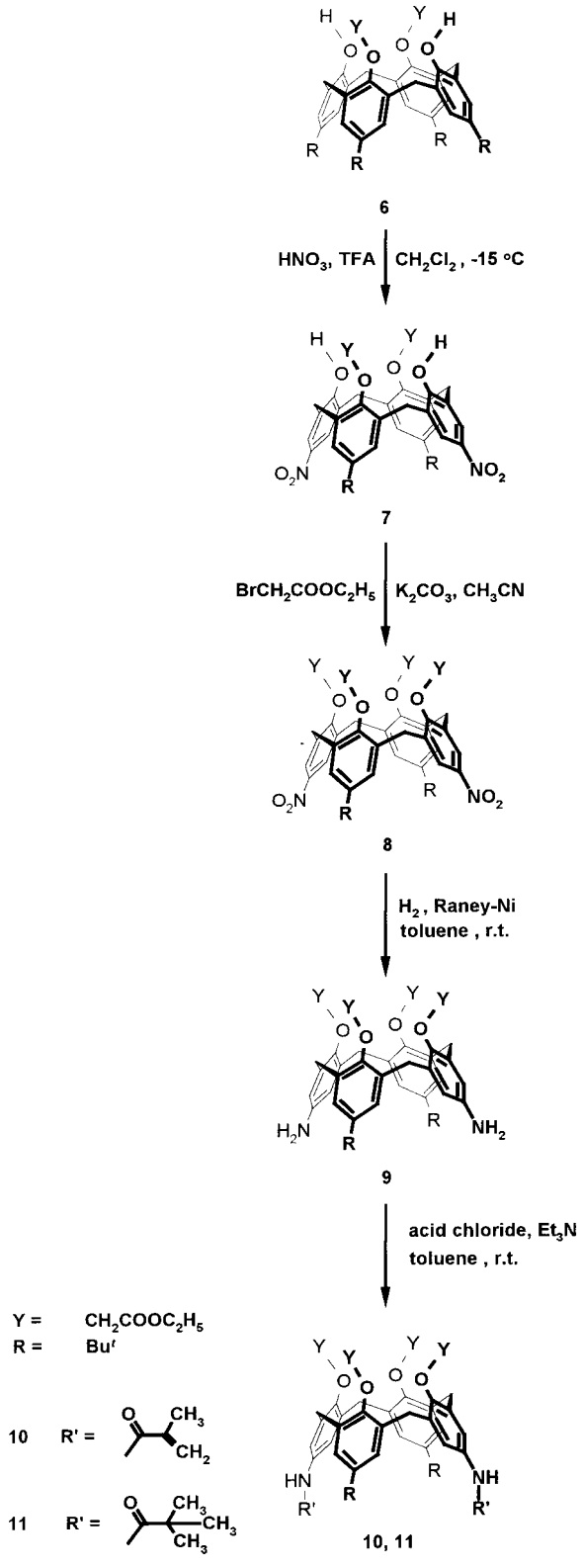
Compounds **2c**, **d** and **8** are of particular interest, since nitro groups are not affected by many chemical reactions. Therefore, hydrolysis of the ester groups of **2c**, **d**, subsequent conversion of the tetraacid to the acid chloride (by reaction with $SOCl_2$) and its reaction with various hydroxy or amino compounds can be used as a universal method for the preparation of different types of calixarene receptors. By this (and similar) reaction sequences tetraester moieties can be converted into a variety of tetraamides,[17] tetrathioamides,[18] *N*-sulfonylcarboxyamides[19] and so on, which subsequently can be transformed into polymerizable methacrylamide derivatives as described above.

Polymer synthesis

The calixarene monomers **4a–d** and **10** were copolymerized with methyl methacrylate. Preliminary syntheses with **4a** and **4b** in dry benzene with benzoyl peroxide as initiator furnished polymers in yields decreasing (in the range of 40 to 95%) with increasing calixarene content in the monomer mixture.

Since **4c** has receptor groups for metal cations its copolymerization was investigated in more detail. We used various amounts of calixarene in the starting mixture (ranging from 1 to 10 mol%). The yields of polymers **P4c** are plotted in Fig. 2 *vs.* the content of **4c** in the monomer mixtures. Again a decrease in the yield of isolated polymer with increasing concentration of **4c** is observed. It may be due to an incomplete conversion of monomers (see below) or to a general change in the solubility of polymers leading to losses during the isolation under standard precipitation conditions.

The constitution of **P4c** as poly(methyl methacrylate-*co*-methacrylamide) was confirmed by the absence of vinylic absorptions in both the IR and NMR spectra and the presence of amide and ester carbonyl absorptions at 1685 and 1730 cm^{-1}, respectively, and of signals for the other calixarene protons in the ^{1}H NMR spectrum. The composition of the obtained polymers was determined by UV–VIS and ^{1}H NMR spectroscopies. The calixarene moieties show an intensive absorption band at 281 nm, which is not present for methyl methacrylate moieties. The calixarene with a pivalamide group (**5c**) was used for calibration.



Scheme 2

Fig. 3 shows that for concentrations up to 5 mol% (35 wt%) of calixarene in the monomer mixture the resulting copolymer composition is almost the same as that of the precursor mixture. For concentrations higher than 5 mol% of monomer **4c** the precipitated polymers contained unreacted **4c**, which was difficult to remove by reprecipitation.

Table 1 summarizes some characteristics of the copolymers. It shows that calixarene-based polymers exhibit high molecular weights, increasing with the concentration of **4c** in the monomer mixture and a polydispersity ($D = M_w/M_n$) between 3 and 5, which is more or less typical for radical polymerizations. The values for $M_n = 40\,000$ to $250\,000$ u correspond to (over all) degrees of polymerization of $D_n = 400$ to 1500 and an average of 4 to 90 calixarene units per polymer molecule. For comparison, D_P of homopolymers obtained from a narrow rim methacrylate derived from tetraester **1c** was in the range of 6–7.[9]

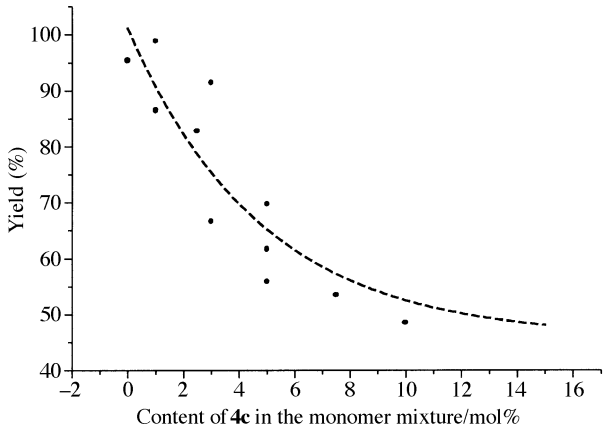


Fig. 2 Dependence of the polymer yield on the composition of the monomer mixture.

The copolymerization of **10** (0.5–5 wt% with methyl methacrylate) gave completely insoluble and crosslinked polymers. This shows that both methacrylamide residues are accessible to radical polymerization.

Extraction and complexation studies

In order to survey the ionophoric properties of the new monomeric and polymeric ligands the extraction of alkali picrates from aqueous solution into dichloromethane was studied. The results are collected in Table 2 and compared with the tetraester **1c** derived from *tert*-butylcalix[4]arene as a standard.[21]

The replacement of one (or two) *tert*-butyl groups by nitro groups leads generally to a strong decrease in the extraction ability of **2c** and **8** (no extraction found at all). Most probably

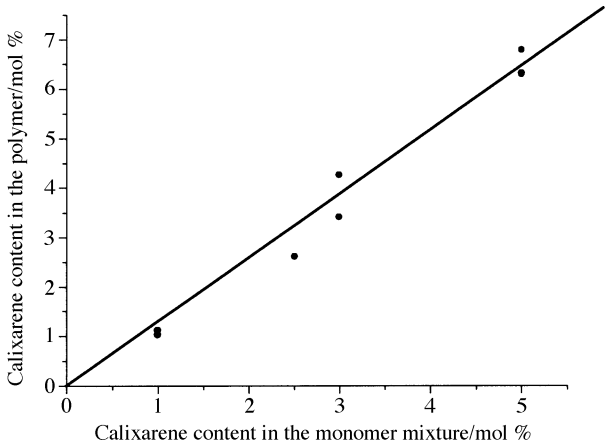


Fig. 3 Composition of the copolymers **P4c** as a function of the concentration of co-monomer **4c**.

Table 1 Characteristics of the calixarene containing polymers

Polymer[a]	$M_w/10^5$ u	$M_n/10^5$ u	D
P4c(1.1)	1.37	0.4	3.3
P4c(3.9)	7.11	1.42	5.0
P4c(6.6)	12.9	2.51	5.1

[a] The content of calixarene units (mol%) is given in parentheses.

Table 2 Extraction of alkali picrates (C_M) from water into dichloromethane by various ligands (C_L) under different concentration conditions at 20 °C

Ligand	Cond.[a]	Li^+	Na^+	K^+	Rb^+	Cs^+
1c[b]	I	7	29	5	4	6
2c	I	<1	<1	<1	<1	<1
4c	I	8 ± 2	15.2 ± 0.4	9 ± 1	8.9 ± 0.2	—
10	I	1.9 ± 0.5	9 ± 1	2.3 ± 0.4	2.0 ± 0.1	—
1c	II	19.6 ± 0.1	55.2 ± 0.1	15.2[c]	13.0[c]	13.7[c]
2c	II	—	2.4 ± 0.1	1.0 ± 0.1	—	—
5c	II	9.1 ± 0.1	34.5 ± 0.1	13.6 ± 0.1	9.4 ± 0.1	7.4 ± 0.1
1c	III	9.2 ± 0.3	44.2 ± 0.1	11.5 ± 0.3	10.1 ± 0.3	15.0 ± 0.7
5c	III	7.8 ± 0.3	29.9 ± 0.1	6.8 ± 0.3	6.9 ± 0.3	4.2 ± 0.3
11	III	9.2 ± 0.3	39.2 ± 0.1	9.2 ± 0.3	8.6 ± 0.3	5.7 ± 0.1
P4c(1.1)[d]	III	14.0 ± 2	29.7 ± 0.1	16.0 ± 1.0	—	—
&4c(6.6)[d]	III	11.1 ± 0.3	31.0 ± 0.6	13.0 ± 0.1	—	—

[a] I: $C_M = 2.5 \times 10^{-4}$ M, $C_L = 2.5 \times 10^{-4}$ M; II: $C_M = 1.25 \times 10^{-4}$ M, $C_L = 1.875 \times 10^{-3}$ M; III: $C_M = 1.25 \times 10^{-4}$ M, $C_L = 9.375 \times 10^{-4}$ M. [b] Previous results, see ref. 20. [c] Formation of a third phase. [d] The content of calixarene units (mol%) is given in brackets.

this is caused by the electron withdrawing properties of the nitro groups, leading to a lower basicity ("donating power") of the phenolic oxygens, although a conformational distortion of the calixarene skeleton cannot be entirely ruled out. However, the amide derivatives **5c** and **10**, which might be distorted in a similar way, show extraction levels roughly comparable with **1c**. The same is true for the polymers **P4c**.

The most important fact is that the selectivity for sodium, a typical property of tetraester **1c**, is essentially unchanged by chemical modification at the wide rim, as anticipated, and is also unaffected by incorporation into the polymer backbone. This is also demonstrated by the complexation constants determined in homogenous solution (MeOH), which reveal an even higher selectivity of the two model compounds **5c** and **11** (especially towards Rb^+ and Cs^+) than for **1c** (Table 3). This is due to distinctly lower complexation constants for these cations (Rb^+, Cs^+) while the values for Na^+ are nearly the same, and those for Li^+ and K^+ show only a slight decrease.

Potentiometric measurements

In order to confirm the complexation ability of the free and the polymer-bound calix[4]arene tetraethyl esters, the selectivity of membranes employing these compounds was investigated. **1c**, **2c**, **4c**, **5c** and **8** as well as two samples of **P4c** were used as ionophores in a PVC–DOS (1 : 2) polymeric matrix. In the latter case the content of calixarene units was the same as the content of free calixarene ionophores. Compositions and working parameters of the tested electrodes are presented in Table 4. The results reveal that all electrodes perform with the theoretical slope for changes in the sodium ion concentration. Among the monomeric calixarenes (**1c**, **2c**, **4c**, **5c** and **8c**) a significant loss in selectivity, towards potassium ions was observed for the nitro derivatives **2c** and **8**. The incorporation of a second nitro group into the ionophore structure (**8**) causes an additional increase of the log $K^{pot}_{Na,K}$ value (−0.9) in comparison to the mononitro derivative **2c** (−1.7). This is in line with the extraction results and can be explained by a stronger electron withdrawing effect of two nitro substituents as compared to one.

However, the most important conclusion that can be drawn from the results obtained for model compound **1c** and calixarene polymers **P4c**(2.6) and **P4c**(6.6) is that immobilization does not diminish the selectivity of the original ionophore. From Fig. 4 it can be seen that the analytically useful linear concentration domain of the calibration curve for sodium ions is unchanged. Moreover, immobilization of the calixarene does not affect the dynamic response of the electrodes. As shown in Fig. 5, the response time of electrodes with membranes doped with **P4c** is as fast as for membranes with the

Table 3 Complexation constants (log $\beta \pm \sigma_{n-1}$) in methanol ($T = 25$ °C, 10^{-2} M Et_4NCl)

Ligands	Li^+	Na^+	K^+	Rb^+	Cs^+
1c[a]	2.6	5.0	2.4	3.1	2.7
5c	1.2 ± 0.7	4.90 ± 0.04	2.24 ± 0.02	1.1 ± 0.2	1.3 ± 0.4
11	2.00 ± 0.0902	5.2 ± 0.3	2.0 ± 0.1	1.36 ± 0.08	0.98 ± 0.03

[a] Previous results, see ref. 13.

Table 4 Compositions and working parameters of electrodes with sodium selective membranes containing monomeric calixarenes (**1c**, **2c**, **4c**, **5c** and **8**) and calixarene ionophores immobilized on a polymer matrix (**P4c**)

	Ionophore/ wt%	KTpClPB/ wt%	DOS/ wt%	PVC/ wt%	Selectivity coefficient log $K^{pot}_{Na,J}$			Slope/ mV per dec
					K^+	Ca^{2+}	Mg^{2+}	
1c	2	0.3	64.7	33	−2.3	−3.4	−4.3	58.2
2c	2	0.3	64.7	33	−1.7	−3.3	−4.3	59.0
4c	2	0.3	64.7	33	−2.4	−3.4	−4.3	58.3
5c	2	0.3	64.7	33	−2.2	−3.4	−4.1	58.3
8	2	0.3	64.7	33	−0.9	−3.4	−3.8	59.0
P4c(2.6)[a,b]	10	0.3	58.7	31	−2.3	−3.3	−4.2	58.2
P4c(6.6)[a,c]	5	0.3	62.7	32	−2.2	−3.3	−4.0	58.1

[a] The content of calixarene units (mol%) is given in parentheses. [b] 21.5 wt% of calix[4]arene units. [c] 42.6 wt% of calix[4]arene units.

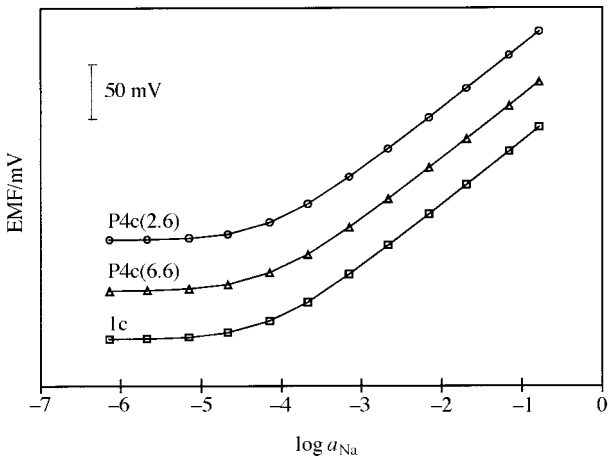


Fig. 4 Potentiometric response curves of sodium selective polymer membrane electrodes based on low molecular weight and on polymeric ionophores; 0.1 M $CaCl_2$ background solution.

free model ionophore and does not exceed a few seconds. It should be mentioned that such membranes based on **P4c** have been tested for a period of 3 months and no significant changes in the electrochemical properties were observed.

Conclusions and outlook

Mono- and dinitro derivatives of calix[4]arene tetraethers, easily available by nitration or ipso-nitration, are versatile starting materials for the synthesis of polymerizable calix[4]arene derivatives, which are obtained for instance by reduction of the nitro groups and acylation with methacryloyl chloride. Copolymerization with methyl methacrylate does not diminish the ionophoric properties of the sodium selective tetraester receptor site at the narrow rim. As anticipated, it is not disturbed by interaction with the polymer chain linked to the wide rim. There is the additional option to attach polymerizable groups *via* suitable spacers. Since the ligating groups attached *via* the ether linkages to the narrow rim may be modified in various ways prior to the introduction of the more sensitive vinyl groups, the outlined strategy allows the synthesis of various polymer-bound ionophores and the preparation of improved ion-sensitive electrodes for various cations.

Experimental

^{1}H NMR spectra were recorded on Bruker AC200 (200 MHz) or AC400 (400 MHz) spectrometers. Chemical shifts are reported as δ values in relative to $(CH_3)_4Si$ as internal standard. FD mass spectra were recorded on a Finnigan MAT 8230; MALDI–TOF mass spectra were recorded on a Kratos Kompact MALDI 4 V5.2.1; IR spectra were recorded on a FTIR Biorad 165 apparatus using KBr pellets. UV–vis measurements were carried out on a HP Lambda 2 in dichloromethane.

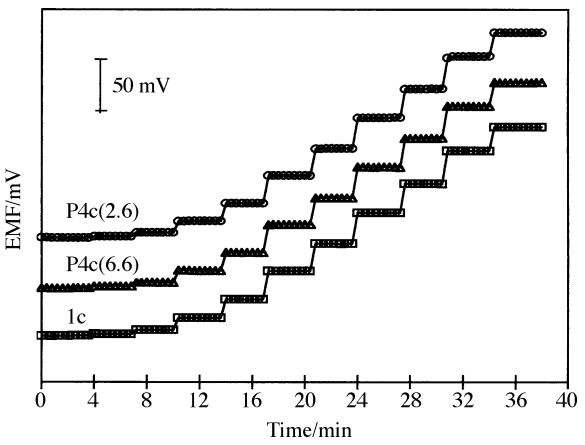


Fig. 5 Dynamic responses of electrodes with ion selective membranes based on low molecular weight and on polymeric ionophores; 0.1 M $CaCl_2$ background solution.

Molecular weights of polymers were determined by gel permeation chromatography (GPC) in THF, using a setup consisting of a LC–10AD pump and Nucleogel 104–5 column. The apparent values reported refer to narrow-polydispersity polystyrene standards. Melting points are uncorrected. Combustion analysis resulted in most cases in C, N values lower than calculated, a phenomenon often encountered with calixarenes. We do not see any point, however, in adjusting these values by arbitrarily chosen fractions of included solvent. All compounds were structurally characterized by ^{1}H NMR and mass spectra; their purity was additionally confirmed by TLC.

Solvents were purified by standard procedures. Compounds **1a**, **1b**, **1c**, **1d** and **6** were prepared according to procedures described in the literature.[20] The preparation of **2b**, **2c**, **3b**, **3c** and **7** was published before.[15,16]

Synthesis of nitro calixarenes

5-Nitro-25,26,27,28-tetrapentyloxycalix[4]arene, 2a. To a vigorously stirred solution of compound **1a** (4 g, 5.68 mmol) in CH_2Cl_2 (340 mL) a mixture of 65% nitric acid (27 mL, 417 mmol) and glacial acetic acid (53.6 mL, 180 mmol) was added. During the reaction the color of the reaction mixture turned to dark purple. After 7 h the reaction mixture was diluted with 150 mL of water. The organic layer was washed with water (3 × 150 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was dissolved in $CHCl_3$–hexane (1 : 2) and filtered over silica. After removal of the solvent the crystallization of the residue from $CHCl_3$–MeOH yielded the pure compound **2a** as a white solid: yield 1.66 g (39%); mp 150–151 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 7.39 (s, 2H, ArH), 7.05–6.96 (m, 6H, ArH), 6.35 (s, 3H, ArH), 4.60 (d, 2H, $ArCH_2Ar$, ax, J = 14 Hz), 4.55 (d, 2H, $ArCH_2Ar$, ax, J = 14 Hz), 4.05–3.85 (m, 8H, OCH_2), 3.33 (d, 2H, $ArCH_2Ar$, eq, J = 14 = Hz), 3.29 (d, 2H, $ArCH_2Ar$, eq, J = 14 Hz), 2.15–1.80 (m, 8H, CH_2), 1.65–1.30 (m, 16H, CH_2), 1.10–1.00 (m, 12H, CH_3); MS (FD): m/z 749.5 (M^+).

11,17,23-Tri-*tert*-butyl-5-nitro-25,26,27,28-tetrakis(methoxycarbonylmethoxy)calix[4]arene, 2d. A vigorously stirred solution of compound **1d** (3.74 g, 4 mmol) in CH_2Cl_2 (200 mL) was cooled in an ice bath to 10 °C and fuming nitric acid (0.95 mL, 13.1 mmol) was added. The ice bath was then removed and the reaction mixture allowed to warm to room temperature. The reaction was followed by TLC (acetone–$CHCl_3$ 2 : 5) and stopped by the addition of water when compound **1d** completely disappeared (~30 min). (Usually the reaction was complete when the mixture reached room temperature). The organic layer was washed several times with water, dried ($NaSO_4$) and the solvent evaporated under reduced pressure. The residue was purified by gel chromatography (ethyl acetate–hexane 1 : 3). After removal of the solvents the addition of MeOH yielded the pure compound **2d** (1.34 g, 36%) as yellowish crystals: mp 136–137 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 7.33 (s, 2H, ArH), 7.07 (br s, 4H, ArH), 6.27 (s, 2H, ArH), 5.05 (d, 2H, OCH_2CO, J = 16.6 Hz), 5.02 (d, 2H, $ArCH_2Ar$, ax, J = 14.3 Hz), 4.81 (d, 2H, OCH_2CO, J = 16.6 Hz), 4.68 (d, 2H, $ArCH_2Ar$, ax, J = 13.7 Hz), 4.68 (s, 2H, OCH_2CO), 4.53 (s, 2H, OCH_2CO), 3.80 (s, 3H, $COOCH_3$), 3.75 (s, 3H, $COOCH_3$), 3.72 (s, 6H, $COOCH_3$), 3.24 (d, 2H, $ArCH_2Ar$, eq, J = 13.7 Hz), 3.21 (d, 2H, $ArCH_2Ar$, eq, J = 14.3 Hz), 1.30 [s, 18H, $(CH_3)_3$], 0.66 [s, 9H, $(CH_3)_3$]; MS (FD): m/z 926.1 (M^+).

5,17-Dinitro-11,23-di-*tert*-butyl-25,26,27,28-tetrakis(ethoxycarbonylmethoxy)calix[4]arene, 8. A solution of compound **7** (2.24 g, 2.93 mmol) in acetonitrile (100 mL) was stirred overnight with K_2CO_3 (4.4 g, 29.3 mmol). To the orange-colored suspension ethyl bromoacetate (3.26 mL, 29.3 mmol) was added and the reaction mixture was heated at 70 °C for 3 days. Then the solid salt was filtrated. After removal of the solvent the crystallization of the residue from CH_2Cl_2–MeOH yielded the pure compound **8** as a white solid (2.11 g, 74%); mp 153–154 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 7.13 (s, 4H, ArH), 7.06 (s, 4H, ArH), 4.92 (d, 4H, $ArCH_2Ar$, ax, J = 13.8 Hz), 4.73 (s, 4H, OCH_2CO), 4.69 (s, 4H, OCH_2CO), 4.29–4.08 (m, 8H, OCH_2), 3.27 (d, 4H, $ArCH_2Ar$, eq, J = 13.8 Hz), 1.32–1.21 (m, 12H, CH_3), 1.28 [s, 18H, $(CH_3)_3$];MS (MALDI-TOF): m/z 972.6 (M^+).

General procedure for the reduction of nitro calixarenes

Compound **2** or **8** was dissolved in toluene (75 mL per mmol), Raney–Nickel was added (~0.5–1 cm^3) and the resulting suspension was vigorously stirred under a hydrogen atmosphere at room temperature. When the hydrogen uptake was finished the suspension was rapidly filtered over sand, washed with warm toluene and the combined organic layers dried over Na_2SO_4. After removal of the solvent under reduced pressure compound **3** was obtained in sufficient purity and immediately used for the subsequent reactions or stored under argon.

5-Amino-25,26,27,28-tetrapentyloxycalix[4]arene, 3a. 2a (0.88 g, 1.17 mmol) yielded compound **3a** (0.81 g, 96%) as a colorless oil; ^{1}H NMR 200 MHz (DMSO-d_6) δ: 7.27–7.10 (m, 3H, ArH), 6.63–6.30 (m, 8H, ArH), 6.12 (s, 2H, NH_2), 4.43 (d, 2H, $ArCH_2Ar$, ax, J = 13.2 Hz), 4.36 (d, 2H, $ArCH_2Ar$, ax, J = 13.0 Hz), 3.94–3.49 (m, 8H, OCH_2), 3.13 (d, 2H, $ArCH_2Ar$, eq, J = 13.0 Hz), 3.04 (d, 2H, $ArCH_2Ar$, eq, J = 13.2 Hz), 1.90–1.70 (m, 8H, CH_2), 1.50–1.10 (m, 16H, CH_2), 1.00–0.80 (m, 12H, CH_3).

5-Amino-11,17,23-tri-*tert*-butyl-25,26,27,28-tetrakis-(methoxycarbonylmethoxy)calix[4]arene, 3d. 2d (0.5 g, 0.54 mmol) yielded compound **3d** (0.36 g, 95%) as a yellow oil; ^{1}H NMR 200 MHz (DMSO-d_6) δ: 8.30 (s, 2H, NH_2), 6.83 (br s, 2H, ArH), 6.74 (br s, 2H, ArH), 6.57 (br s, 4H, ArH), 5.88 (s, 2H, ArH), 4.70–4.40 (m, 12H, OCH_2 and $ArCH_2Ar$ ax), 3.68 (s, 3H, $COOCH_3$), 3.65 (s, 3H, $COOCH_3$), 3.64 (s, 6H, $COOCH_3$), 3.15 (d, 2H, $ArCH_2Ar$, eq, J = 13.2 Hz), 2.94 (d, 2H, $ArCH_2Ar$, eq, J = 12.9 Hz), 1.09 [s, 18H, $(CH_3)_3$], 0.93 [s, 9H, $(CH_3)_3$].

5,17-Diamino-11,23-di-*tert*-butyl-25,26,27,28-tetrakis-(ethoxycarbonylmethoxy)calix[4]arene, 9. 8 (0.47 g, 0.5 mmol) yielded compound **9** (0.43 g, 93%) as a white oil; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 7.17 (s, 4H, NH_2), 7.07 (s, 4H, ArH), 5.65(s, 4H, ArH), 4.79 (d, 4H, $ArCH_2Ar$, ax, J = 14.1 Hz), 4.76 (s, 4H, OCH_2CO), 4.41 (s, 4H, OCH_2CO), 4.26–4.07 (m, 8H, OCH_2), 3.11 (d, 4H, $ArCH_2Ar$, eq, J = 14.1 Hz), 1.36 [s, 18H, $(CH_3)_3$], 1.33–1.18 (m, 12H, CH_3).

General procedure for the preparation of amides 4, 5, 10 and 11 from the corresponding amino compounds

To a stirred solution of the amine (1 mmol of NH_2 groups) and triethylamine (1.15 mmol) in dry toluene (25 mL) the acid chloride (1.05 mmol) was added dropwise under argon. The reaction mixture was stirred for 7 h and then the precipitate was removed by filtration. The solution was washed with water (2 × 15 mL) and dried over Na_2SO_4. After removal of the solvent the recrystallization of the residue from MeOH yielded the pure amides as white solids.

5-Methacrylamido-25,26,27,28-tetrapentyloxycalix[4]-arene, 4a. Yield 92%; mp 129–130 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 7.02 (s, 1H, NH), 6.68 (s, 3H, ArH), 6.60–6.40 (m, 8H, ArH), 5.62 (s, 1H, $=CH_2$), 5.31 (s, 1H, $=CH_2$), 4.37 (d, 2H, $ArCH_2Ar$, ax, J = 13.2 Hz), 4.36 (d, 2H, $ArCH_2Ar$, ax, J = 13.2 Hz), 3.90–3.70 (m, 8H, OCH_2), 3.08 (d, 2H, $ArCH_2Ar$, eq, J = 13.2 Hz), 3.07 (d, 2H, $ArCH_2Ar$, eq, J = 13.2 Hz), 1.94 (s, 3H, CH_3), 1.95–1.75 (m, 8H, CH_2), 1.45–1.20 (m, 16H, CH_2), 0.95–0.81 (m, 12H, CH_3); MS (FD): m/z 788.1 (M^+).

5-Methacrylamido-11,17,23-tri-*tert*-butyl-25,26,27,28-tetrapentyloxycalix[4]arene, 4b. Yield 96%; mp 109–110 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 7.05–6.95 (m, 4H, ArH), 6.59 (s, 1H, NH), 6.44 (s, 2H, ArH), 6.15 (s, 1H, ArH), 5.43 (s, 1H, $=CH_2$), 5.20 (s, 1H, $=CH_2$), 4.36 (d, 2H, $ArCH_2Ar$, ax, J = 13.2 Hz), 4.34 (d, 2H, $ArCH_2Ar$, ax, J = 13.2 Hz), 4.00–3.90 (m, 4H, OCH_2), 3.70–3.55 (m, 4H, OCH_2), 3.04 (d, 4H, $ArCH_2Ar$, eq, J = 13.2 Hz), 1.82 (s, 3H, CH_3), 1.90–1.75 (m, 8H, CH_2), 1.30 (s, 18H, $C(CH_3)_3$), 1.50–1.15 (m, 16H, CH_2), 0.92–0.80 (m, 12H, CH_3), 0.65 [s, 9H, $C(CH_3)_3$]; MS (FD): m/z 956.5 (M^+).

5-Methacrylamido-11,17,23-tri-*tert*-butyl-25,26,27,28-tetrakis(ethoxycarbonylmethoxy)calix[4]arene, 4c. Yield 94%; mp 177–178 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 6.97 (br s, 4H, ArH), 6.69 (s, 1H, NH), 6.54 (s, 2H, ArH), 6.21 (s, 2H, ArH), 5.46 (s, 1H, $=CH_2$), 5.23 (s, 1H, $=CH_2$), 4.88 (s, 4H, OCH_2CO), 4.83 (d, 2H, $ArCH_2Ar$, ax, J = 13.6 Hz), 4.76 (d, 2H, $ArCH_2Ar$, ax, J = 12.6 Hz), 4.52 (s, 2H, OCH_2CO), 4.45 (s, 2H, OCH_2CO), 4.21–4.04 (m, 8H, $COOCH_2$), 3.14 (d, 2H, $ArCH_2Ar$, eq, J = 13.6 Hz), 3.11 (d, 2H, $ArCH_2Ar$, eq, J = 12.6 Hz), 1.84 (s, 3H, CH_3), 1.23 [s, 18H, $(CH_3)_3$], 1.3–1.16 (m, 12H, CH_3), 0.68 [s, 9H, $(CH_3)_3$]; MS (FD): m/z 1022.3 (M^+).

5-Methacrylamido-11,17,23-tri-*tert*-butyl-25,26,27,28-tetrakis(methoxycarbonylmethoxy)calix[4]arene, 4d. Yield 95%; mp 167–168 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 6.98 (br s, 4H, ArH), 6.69 (s, 1H, NH), 6.56 (s, 2H, ArH), 6.23 (s, 2H, ArH), 5.46 (s, 1H, $=CH_2$), 5.23 (s, 1H, $=CH_2$), 4.89 (s, 4H, OCH_2CO), 4.78 (d, 2H, $ArCH_2Ar$, ax, J = 13.2 Hz), 4.74 (d, 2H, $ArCH_2Ar$, ax, J = 13.6 Hz), 4.54 (s, 2H, OCH_2CO), 4.47 (s, 2H, OCH_2CO), 3.74 (s, 3H, $COOCH_3$), 3.70 (s, 3H, $COOCH_3$), 3.66 (s, 6H, $COOCH_3$), 3.15 (d, 2H, $ArCH_2Ar$, eq, J = 13.6 Hz), 3.13 (d, 2H, $ArCH_2Ar$, eq, J = 13.2 Hz), 1.84 (s, 3H, CH_3), 1.23 [s, 18H, $(CH_3)_3$], 0.69 [s, 9H, $(CH_3)_3$]; MS (FD): m/z 964.4 (M^+).

5-Pivalamido-11,17,23-tri-*tert*-butyl-25,26,27,28-tetrakis-(ethoxycarbonylmethoxy)calix[4]arene, 5c. Yield 94%; mp 184–185 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 7.04 (br s, 4H, ArH), 6.57 (s, 1H, NH), 6.52 (s, 2H, ArH), 6.25 (s, 2H, ArH), 4.94 (s, 4H, OCH_2CO), 4.86 (d, 2H, $ArCH_2Ar$, ax, J = 12.7 Hz), 4.81 (d, 2H, $ArCH_2Ar$, ax, J = 13.2 Hz), 4.56 (s, 2H, OCH_2CO), 4.47 (s, 2H, OCH_2CO), 4.26–4.08 (m, 8H, $COOCH_2$), 3.19 (d, 2H, $ArCH_2Ar$, eq, J = 13.2 Hz), 3.16 (d, 2H, $ArCH_2Ar$, eq, J = 12.7 Hz), 1.28 [s, 18H, $(CH_3)_3$], 1.34–1.20 (m, 12H, CH_3), 1.12 [s, 9H, $(CH_3)_3$], 0.74 [s, 9H, $(CH_3)_3$]; MS (FD): m/z 1036.8 (M^+).

5,17-Dimethacrylamido-11,23-di-*tert*-butyl-25,26,27,28-tetrakis(ethoxycarbonylmethoxy)calix[4]arene, 10. 9 (0.43 g, 0.47 mmol) yielded 0.47 g (95%) of compound **10** as a white solid; mp 171–172 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 7.09 (s, 2H, NH), 6.95 (s, 4H, ArH), 6.39 (s, 4H, ArH), 5.46 (s, 2H, $=CH_2$), 5.17 (s, 2H, $=CH_2$), 4.80 (s, 4H, OCH_2CO), 4.80 (d, 4H, $ArCH_2Ar$, ax, J = 13.7 Hz), 4.51 (s, 4H, OCH_2CO), 4.18–4.05 (m, 8H, $COOCH_2$), 3.15 (d, 4H, $ArCH_2Ar$, eq, J = 13.7 Hz), 1.80 (s, 6H, CH_3), 1.22 [s, 18H, $(CH_3)_3$], 1.30–1.10 (m, 12H, CH_3); MS (FD): m/z 1047.3 (M^+).

5,17-Dipivalamido-11,23-di-*tert*-butyl-25,26,27,28-tetrakis-(ethoxycarbonylmethoxy)calix[4]arene, 11. **9** (0.6 g, 0.66 mmol) yielded 0.51 g (73%) of compound **11** as a white solid; mp 188–189 °C; ^{1}H NMR 200 MHz ($CDCl_3$) δ: 7.08 (s, 2H, NH), 6.87 (s, 4H, ArH), 6.80 (s, 4H, ArH), 4.84 (d, 4H, $ArCH_2Ar$, ax, J = 13.3 Hz), 4.78 (s, 4H, OCH_2CO), 4.76 (s, 4H, OCH_2CO), 4.28–4.15 (m, 8H, $COOCH_2$), 3.20 (d, 4H, $ArCH_2Ar$, eq, J = 13.3 Hz), 1.35–1.15 (m, 12H, CH_3), 1.22 [s, 18H, $(CH_3)_3$], 1.10 [s, 18H, $(CH_3)_3$]; MS (MALDI-TOF): m/z 1079.7 (M^+).

General procedure for the copolymerization of 4

The solution of **4** and methyl methacrylate (totaling 2 mmol) in 0.23 mL of dry benzene (containing 1 wt% of benzoyl peroxide) was placed in a small flask. When **4** was dissolved, nitrogen was passed through the solution to remove the oxygen and the flask was closed and thermostated at 80 °C for 48 h. The viscous solution was diluted with 1 mL of dichloromethane and then poured with stirring into 7 mL of hexane. The precipitated polymer was filtered and dried.

Extraction and complexation studies

Extraction of alkali picrates from an aqueous solution (C_M) into a solution of calixarene (C_L) in dichloromethane was performed at 20 °C according to the procedure previously published.[21] Unless otherwise stated, the concentrations C_M and C_L were 1.25×10^{-4} M and 9.375×10^{-3} M, respectively.

The stability constants were determined at 25 °C by spectrophotometric titration of the calixarene with the metal ion in methanol. The ionic strength was held constant at 10^{-2} M by use of tetraethylammonium chloride. The experimental procedure, the nature and origin of the chemicals used and the method of interpretation of the measurements have been reported in detail earlier.[21]

Evaluation of Na^+ selective electrodes

Materials and reagents. Potassium tetrakis(4-chlorophenyl) borate (KTpClPB), bis(2-ethylhexyl) sebacate (DOS), high molecular weight poly(vinyl chloride) (PVC) and tetrahydrofuran (THF, distilled prior to use) were purchased from Fluka (Ronkonkoma, NY). All aqueous solutions were prepared with salts of the highest purity available using distilled-deionized water.

Membrane preparation. For membrane compositions see Table 4. In general, they contained 2 wt% of calixarene units, 30 mol% KTpClPB (relative to calixarene units) in a PVC–DOS (1 : 2) polymeric matrix. The membrane components, total 200 mg, were dissolved in 2 ml of freshly distilled THF. This solution was placed in a glass ring (24 mm i.d.) on a glass plate. After solvent evaporation the resulting membrane was peeled from the glass mold and discs of 7 mm diameter were cut out. Membrane discs were mounted in conventional ISE electrode bodies (Type IS 561; Philips, Eindhoven) for EMF measurements. For each membrane composition two electrodes were prepared.

EMF measurements. All measurements were performed at ambient temperature (22 ± 1 °C) using a galvanic cell of the type: Ag/AgCl/3M KCl/1 M CH_3COOLi/sample/membrane/0.01 M NaCl/AgCl/Ag. The EMF values were measured using a custom made 16-channel electrode monitor. Details of this equipment were described previously.[22] Potentiometric selectivity coefficients were determined according to the fixed interference method (FIM) using 0.1 M (for Ca^{2+} or Mg^{2+}) and 0.01 M (for K^+) solutions of the interfering ion.[23] Activity coefficients were calculated according to the Debye–Hückel approximation.[24] The calibration of the electrodes was examined in solutions containing a background of interfering cations of appropriate concentration over the concentration range of 10^{-7}–10^{-1} M of Na^+ ions.

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