Monatshefte für Chemie 129, 1169–1181 (1998)

**Monatshefte für Chemie**
**Chemical Monthly**

Printed in Austria

# Calix[4]amidocrowns and Calix[4]amidocryptands Bridged at the Wide Rim

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**Summary.** New macrobicyclic calix[4]amidocrowns (**9–12**) and macrotricyclic calix[4]amidocryptands (**13**, **14**) have been obtained by reaction of a calix[4]arene derivative containing two distal acid chloride groups at the wide rim (**8**) with appropriate diamines. Their ionophoric properties were checked in PVC membranes. The calix[4]amidocrowns **10–12** did not alter significantly the selectivity of the membranes towards different alkali metal and alkaline earth metal cations. The calix[4]amidocryptands **13** and **14**, however, showed significant $Li^+$ over $Na^+$ selectivity, especially derivative **13** with the smaller 15-membered diazacrown moiety.

**Keywords.** Calix[4]arenes; Calix[4]amidocrowns; Calix[4]amidocryptands; Ionophoric properties.

**Am weiteren Rand verbrückte Calix[4]amidokronen und Calix[4]amidokryptanden**

**Zusammenfassung.** Durch Reaktion eine Calix[4]arenderivates mit zwei gegenüberliegenden Säurechloridfunktionen am weiteren Rand (**8**) mit geeigneten Diaminen wurden neue macrobicyclische Calix[4]amidokronen (**9–12**) und macrotricyclische Calix[4]amidokryptanden (**13**, **14**) erhalten. Ihre Eigenschaften als Ionophore wurden in PVC-Membranen untersucht. Im Vergleich mit der reinen Membran bewirkten die Verbindungen **10–12** keine signifikante Änderung der Membranselektivität gegenüber verschiedenen Alkali- und Erdalkalikationen. **13** und **14** zeigten jedoch eine signifikante Selektivität von $Li^+$ über $Na^+$, insbesondere das Derivat **13** mit dem kleineren, 15-gliedrigen Diazakronenether.

## Introduction

Calix[4]arenes [1] have been frequently used as molecular scaffold for the construction of ionophores [2]. In most cases, suitable ligating functions have been attached to the hydroxy groups at the narrow rim. Numerous ligands of the podand type [3] have been obtained in this way, but also more sophisticated macrobicyclic

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molecules like calixcrowns [4] or calixspherands [5], which show hitherto unknown selectivity [6] or (kinetic) stability [7].

Ionophores obtained by modification of the wide rim have been explored less frequently [8], although *t*-butylcalix[4]arene has been shown to encapsulate $Cs^+$ ions in the crystalline state [9]. This demonstrates that the calix[4]arene cavity itself may act as ligating side for suitable cations. First examples for wide rim calix[4]crowns, based on benzylether structures [10], did not show remarkable complexing properties. More recently, wide rim calix[4]crowns with hydroquinone structures have been synthesized [11] which can be "fine tuned" by the substituents in the remaining *p*-positions to complex either alkylammonium ions or alkali metal cations [12].

In the present paper we describe the synthesis of some new calix[4]arene derivatives in which two distal positions at the wide rim [13] are connected *via* diamido oligo(oxyethylene) chains (calix[4]amidocrowns) or *via* diamido crown ether fragments (calix[4]amidocryptands) as well as some ionophoric properties of these compounds.

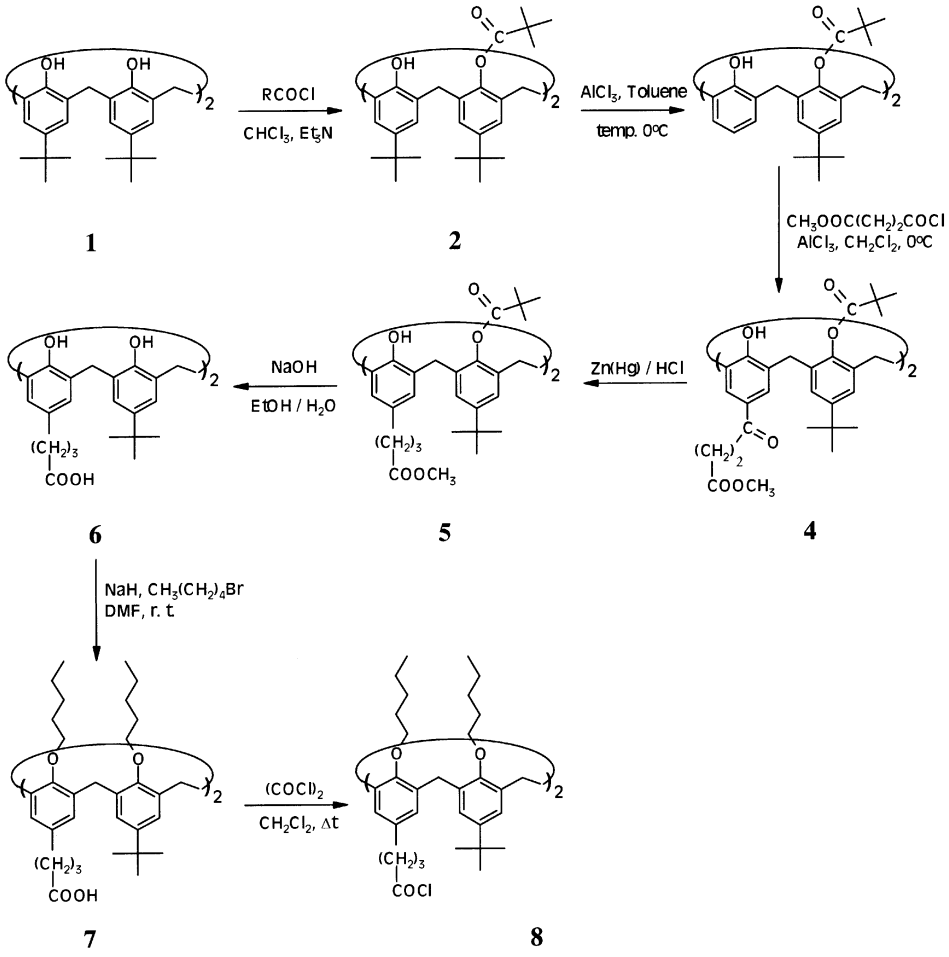
## Results and Discussion

### *Synthesis of ionophores*

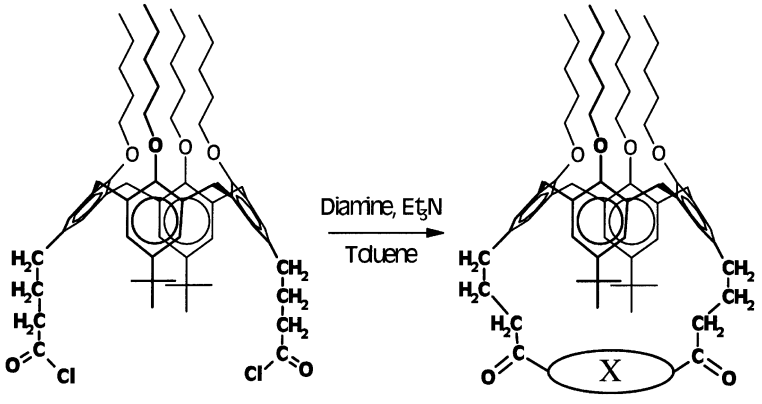
Our strategy for the synthesis of the new calix[4]amidocrowns **8**–**12** and calix[4]-amidocryptands **13** and **14** bridged at the wide rim is based on the reaction of diacid dichloride **8** with linear or cyclic diamines. The synthesis of the diacid dichloride **8** is outlined in Scheme 1.

Diester **2** was obtained by reaction of *p-tert*-butylcalix[4]arene (**1**) [14] with pivaloyl chloride according to the procedure described by *Gutsche et al.* [15]. When a strong base like triethylamine was used, the yield of **2** was almost quantitative. The diester **2** was selectively dealkylated, and the resulting compound **3** was acylated by reaction with 4-methoxy-4-oxybutanoyl chloride under typical *Friedel-Crafts* conditions to give the diketone **4** in high yield (89%). *Clemmensen* reduction of the carbonyl group finally led to **5** (77%). To improve the solubility of the final products and to protect the OH groups during the formation of the diacid dichloride, four pentyl substituents were introduced at the narrow rim of the calix[4]arene. We have found that the best way to get such tetraethers in the cone conformation in high yield is the stepwise addition of small portions of NaH and pentyl bromide to the solution of calixarene **6** in dry *DMF*, rather than the simultaneous addition of the alkylating agent and base in one portion. In the latter case, the yield of tetraether was much lower (10–25%). Subsequent reaction of diacid **7** with oxalyl chloride in $CH_2Cl_2$ gave the corresponding diacid dichloride **8** in almost quantitative yield; **8** was used immediately for the reaction with an appropriate diamine.

The macrocyclization step (Scheme 2) was carried out under high dilution by slow simultaneous addition of both reagents to a solution of triethylamine in dry toluene. After evaporation of the solvent, the crude product was purified by flash chromatography [16]. The diamines used and the products isolated are summarized in Table 1 (see Experimental). It was found that, similar to the synthesis of bicyclic




**Scheme 1.** Synthesis of diacid dichloride **8**




**Scheme 2.** Macrocyclization step of diacid dichloride **8**

and tricyclic calix[4]arenes with bridges at the narrow rim, no double or triple calixarenes were isolated, although their formation cannot be entirely excluded.

The $^1$H NMR spectra of compounds **9**–**14** can be fully assigned in agreement with the proposed structures. The main spectroscopic features are one singlet for the *tert*-butyl protons, two singlets for the aromatic protons, and two doublets for protons of the $ArCH_2Ar$ bridges, indicating the equivalence of all four methylene groups. In the case of compounds **8**–**12**, a broad signal for the NH protons can also be observed. The multiplet for the methylene protons of the bridge is usually sharply defined, but they always coincide with one triplet for the $OCH_2$ protons of the ether parts, and for this reason it is difficult to assign all signals in this region unequivocally. In the case of compounds **13** and **14** this region is less clearly defined, and the signals for the methylene protons of azacrown fragments are very broad, especially those of **13**.

It is interesting that – in spite of the unsymmetrical structure of azacrown [2.1] used as a starting material – the resulting calix[4]amidocryptand **13** has a relatively simple $^1$H NMR spectrum. It shows only one singlet for the *tert*-butyl groups, a single pair of doublets for the methylene bridge, and two singlets for aromatic protons. This can be explained by the length and the flexible nature of two spacers between the calixarene and azacrown moieties which allow a time averaged symmetrical arrangement of the azacrown ether ring with respect to the calixarene.

### *Selectivities of ionophores*

Membrane techniques are particularly suitable for a rapid screening of macrocyclic ligand selectivities towards inorganic ions or organic species. A necessary and important prerequisite is a sufficient lipophilicity of the supramolecular system which allows the ligand to remain in a polymer membrane. Therefore, it is also a practical test for the ionophore's usefulness as a sensing component in ion selective membranes.

Provided that the ion selectivity of the membrane is related to the free energy of transfer of ions from a water phase to the membrane phase, this selectivity depends on the selectivity behavior of the ionophore used, which can be fully specified by the values of complex stability constants, and on the membrane composition (the concentration of free ligands and lipophilic counter-ions as well as the extraction properties of the membrane solvent).

The ionophores **10**–**14** were evaluated in PVC plasticized membranes (for composition, see Experimental) mounted in electrode bodies and then conditioned in a diluted aqueous solution of sodium chloride. The logarithmic values of the selectivity coefficients $\log K^{Pot}$ are presented in Fig. 1. The calix[4]amidocrown derivatives (ionophores **10**–**12**) do not alter significantly the selectivity of the membrane towards different alkali metal and alkaline earth cations in comparison to the blank membrane. Longer conditioning of the membrane from two to nine days in NaCl solution did not change their selectivity patterns.

The calix[4]amidocryptands derivatives (ionophores **13** and **14**) have shown significant $Li^+$ over $Na^+$ selectivity, especially derivative **13** with the smaller 15-membered diazacrown moiety (see Fig. 1). The lithium cation is less lipophilic than sodium, but due to the high $Li^+$-selectivity of the ionophore present in the

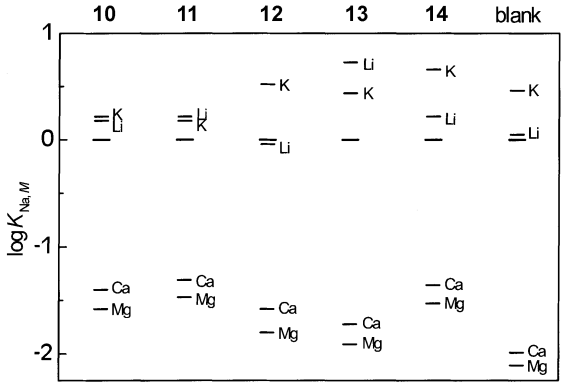



**Fig. 1**. Values of selectivity coefficients $\log K_{Na,M}$; conditions: $10^{-2}\,M$ MCl, $pH = 6$; internal electrolyte: $10^{-2}\,M$ NaCl, $pH = 6$; membranes were conditioned for two days in $10^{-2}\,M$ NaCl, $pH = 6$

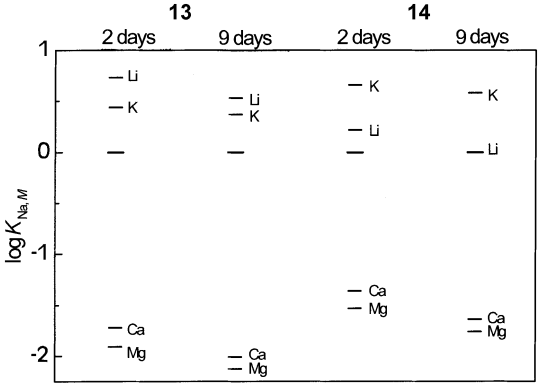



**Fig. 2**. Influence of conditioning time on the selectivity coefficients $\log K_{Na,M}$; conditions: $10^{-2}\,M$ MCl, $pH = 6$; internal electrolyte: $10^{-2}\,M$ NaCl, $pH = 6$; membranes were conditioned for two and nine days in $10^{-2}\,M$ NaCl, $pH = 6$

membrane, the activity of lithium ions in the membrane is higher than that of sodium ions. The observed $Li^+$-selectivity of the membrane based on this calix[4]amidocryptand derivative sustained even during longer conditioning of the membrane in NaCl solution (Fig. 2).

In order to verify the independence of the $Li^+$-selectivity from the kind of the internal electrolyte, new membranes were mounted in electrode bodies with lithium chloride as an internal electrolyte and then conditioned in diluted aqueous solution of LiCl. Figure 3 proves that $Li^+$-selectivity of the membrane does not depend on the membrane treatment and that it is caused by the high $Li^+$-selectivity of ionophore **13**.

It appears that the change of the cap at the wide rim of calix[4]arene derivatives from poly(oxyethylene) chains to azacrown moieties significantly increases the selectivity for lithium over sodium cations. Further work in this direction is being pursued.

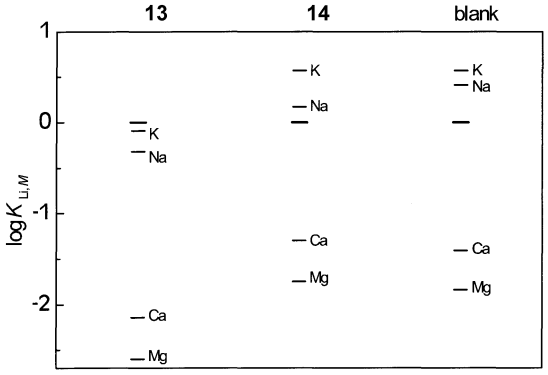



**Fig. 3**. Values of selectivity coefficients $\log K_{\mathrm{Li},M}$; conditions: $10^{-2}\,M$ MCl, $pH = 6$; internal electrolyte: $10^{-2}\,M$ LiCl, $pH = 6$; membranes were conditioned for two days in $10^{-2}\,M$ LiCl, $pH = 6$

## Experimental

$^1$H and $^{13}$C NMR spectra were recorded on a Varian VXR 300 spectrometer using $2.5\times10^{-3}\,M$ solutions in $CDCl_3$ (except of **5** for which the spectrum was recorded in *DMSO*-$d_6$). Chemical shifts are reported as $\delta$ values relative to internal *TMS*. The melting points reported are uncorrected. Values higher than 200°C were determined in sealed capillary tubes under argon. FD mass spectra were recorded on a CH 7A Varian MAT instrument. All compounds were checked for purity by thin layer chromatography on silica gel plates of 0.25 mm thickness (E. Merck, 70–230 mesh ASTM). Silica gel (E. Merck Silica Gel 60, 40–63 μm) was used for column chromatography. All solvents were purified and dried by standard procedures. All solutions were dried over $Na_2SO_4$. Most starting materials were purchased from Merck. *p-tert*-Butylcalix[4]arene (**1**) was prepared according to the literature procedure [14]. Elemental analyses agreed with the calculated values within experimental errors.

*25,27-Bis(2,2-dimethylpropionyloxy)-26,28-dihydroxy-p-tert-butylcalix[4]arene* (**2**; $C_{54}H_{72}O_6$)

To 20 g (27 mmol) of a suspension of the complex *p-tert*-butylcalix[4]arene/toluene in 600 ml of dry chloroform, 10.92 g (108 mmol) of $Et_3N$ and then 19.6 g (162 mmol) of pivaloyl chloride were added. The resulting mixture was stirred at room temperature for 24 h; then ice/water (100 ml) was added. The organic layer was separated, washed with water, dried, and evaporated to a volume of about 100 ml. The product was precipitated with 100 ml of methanol and left in a refrigerator. The tiny white crystals were filtered off, washed with small portions of cold methanol and dried to give 27.5 g (99%) of **2**.

M.p.: >350°C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 0.85$ (s, 18H, $C(CH_3)_3$), 1.33 (s, 18H, $C(CH_3)_3$), 1.54 (s, 18H, $C(CH_3)_3$), 3.30 and 3.85 (2d, $J = 13.8$ Hz, 4H each, $ArCH_2Ar$), 5.56 (s, 2H, OH), 6.69 (s, 4H, ArH), 7.11 (s, 4H, ArH) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 27.45$, 30.80, 31.67 ($C(CH_3)_3$), 31.40 ($ArCH_2Ar$), 33.85, 33.93, 39.56 ($C(CH_3)_3$), 125.3, 125.55, 127.96, 131.01, 141.95, 142.62, 148.36, 150.17 (Ar), 176.66 (C=O) ppm.

*5,11-Di-p-tert-butyl-25,27-bis(2,2-dimethylpropionyloxy)-26,28-dihydroxycalix[4]arene* (**3**; $C_{46}H_{56}O_6$)

To a solution of 20 g of **2** in 750 ml of dry toluene, $AlCl_3$ (88 g, 0.66 mmol) was added in one portion. The resulting red suspension was stirred for two hours at room temperature (the disappearance of **1** and monodealkylated product was controlled by TLC). After completion of the reaction the mixture

was poured on ice/water (approx. 1000 g). When the color had turned to yellow, the organic layer was separated, and the aqueous phase was extracted with two portions of toluene. The combined toluene solutions were washed twice with water, dried, and evaporated to yield a red oil. After trituration with 100 ml of methanol a white precipitate was formed which was filtered off. Recrystallization of the crude product from chloroform/methanol gave 15.4 g (89%) of pure **3** as white crystals after drying.

M.p.: 320°C (dec); $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 0.88$ (s, 18H, $C(CH_3)_3$), 1.54 (s, 18H, $C(CH_3)_3$), 3.34 and 3.84 (2d, $J = 13.9$ Hz, 4H each, $ArCH_2Ar$), 5.72 (s, 2H, OH), 6.70 (s, 4H, ArH), 6.77 (t, $J = 7.4$ Hz, 2H, ArH), 7.10 (t, $J = 7.4$ Hz, 2H, ArH) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 27.48$, 30.96 ($C(CH_3)_3$), 31.46 ($ArCH_2Ar$), 33.93, 39.55 ($C(CH_3)_3$), 119.7, 125.68, 128.45, 128.65, 130.82, 142.28, 148.67, 152.69 (Ar), 176.60 (C=O) ppm.

*5,11-Di-p-tert-butyl-17,23-bis(4-methoxy-4-oxobutanoyl)-25,27-bis(2,2-dimethyl-propionyloxy)-26,28-dihydroxycalix[4]arene* (**4**; $C_{56}H_{68}O_{12}$)

27.7 g (208.1 mmol) of $AlCl_3$ and afterwards 8.6 ml (83.7 mmol) of 4-methoxy-4-oxobutanoyl chloride were added to 430 ml of dry $CH_2Cl_2$ at 0°C. The mixture was stirred for 10 min; then 14.3 g (20.3 mmol) of **3** were added in one portion. After 2 h stirring at 0–5°C, 500 g of ice/water were added. The organic layer was separated, washed with cold water and brine, dried, and evaporated to dryness. After recrystallization from chloroform/methanol, pure **4** (16.9 g, 89%) was obtained as white crystals.

M.p.: 311–313°C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 0.86$ (s, 18H, $C(CH_3)_3$), 1.52 (s, 18H, $C(CH_3)_3$), 2.73 (t, $J = 6.8$ Hz, 4H, $CH_2$), 3.29 (t, $J = 6.8$ Hz, 4H, $CH_2$), 3.43 and 3.81 (2d, $J = 14.2$ Hz, 4H each, $ArCH_2Ar$), 3.7 (s, 6H, $OCH_3$), 6.42 (s, 2H, OH), 6.70 (s, 4H, ArH), 7.81 (s, 4H, ArH) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 27.48$, 30.96 ($C(CH_3)_3$), 31.46 ($ArCH_2Ar$), 33.93, 39.55 ($C(CH_3)_3$), 119.7, 125.68, 128.45, 128.65, 130.82, 142.28, 148.67, 152.69 (Ar), 176.60 (C=O) ppm.

*5,11-Di-p-tert-butyl-17,23-bis(4-methoxy-4-oxobutyl)-25,27-bis(2,2-dimethyl-propionyloxy)-26,28-dihydroxycalix[4]arene* (**5**; $C_{56}H_{72}O_{10}$)

To Zn amalgam [17] prepared from 30 g of Zn, 6 ml of water, 45 ml of conc. HCl, 60 ml of toluene, and 8 g (8.58 mmol) of **4** were added. The resulting mixture was refluxed for 24 h, an additional quantity of 10 ml of conc. HCl being added after 12 h. After cooling the solution was decanted, and the remaining zinc was powdered and extracted three times with hot toluene. The combined organic solutions were washed three times with cold water, dried, concentrated almost to dryness, and the product was precipitated by the addition of 100 ml cold methanol. The crude product was filtered off and recrystallized from $CHCl_3$/MeOH to give 6 g (77%) of **5** as a white crystals.

M.p.: 226–227°C; $^1$H NMR ($CDCl_3$, 300 MHz) : $\delta = 0.86$ (s, 18H, $C(CH_3)_3$), 1.52 (s, 18H, $C(CH_3)_3$), 1.90 (m, 4H, $CH_2CH_2CH_2$), 2.32 (t, $J = 7.4$ Hz, 4H, $ArCH_2CH_2CH_2$), 2.27 (t, $J = 6.9$ Hz, 4H, $ArCH_2CH_2CH_2$), 3.29 and 3.83 (2d, $J = 13.8$ Hz, 4H each, $ArCH_2Ar$), 2.60 (s, 6H, $COOCH_3$), 5.57 (s, 2H, OH), 6.62 (s, 4H, aromatic), 6.91 (s, 4H, aromatic) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 27.49$, 30.91 ($C(CH_3)_3$), 27.08, 32.97, 34.08 (-$CH_2$-), 33.89, 39.56 ($C(CH_3)_3$), 51.35 ($COOCH_3$), 125.6, 128.54, 128.64, 130.96, 132.46, 142.27, 148.64, 150.94 (Ar), 173.91 ($COOCH_3$), 176.61 ($(CH_3)_3COO$) ppm.

*5,11-Di-p-tert-butyl-17,23-bis(3-carboxypropyl)-25,26,27,28-tetrahydroxycalix[4]arene* (**6**; $C_{44}H_{52}O_8$)

To a solution of 5.1 g (127 mmol) of NaOH in 60 ml ethanol and 40 ml water, 7.2 g (7.96 mmol) of **5** were added in one portion. The suspension was heated and stirred for 24 h under reflux. After cooling, the reaction mixture was diluted with 150 ml water, and 90 ml of 3 N HCl were added. The

precipitated product was filtered off and washed with ethanol/water to remove all pivalic acid. The crude product was then air dried and used for the subsequent reaction without further purification.

Yield: 5.1 g (90%); m.p.: 291–293°C; $^1$H NMR (*DMSO*-$d_6$, 300 MHz): $\delta = 1.16$ (s, 18H, $C(CH_3)_3$), 1.65 (m, 4H, $CH_2CH_2CH_2$), 2.11 (t, $J = 7.4$ Hz, $ArCH_2CH_2CH_2$), 2.28 (t, $J = 7.9$ Hz, $ArCH_2CH_2CH_2$), 3.50 and 3.83 (2×br, 4H each, $ArCH_2Ar$), 6.92 (s, 4H, ArH), 7.14 (s, 4H, ArH), 9.81 (br, 4H, OH) ppm; $^{13}$C NMR (*DMSO*-$d_6$, 75 MHz): $\delta = 25.99$, 33.19, 33.74 ($C(CH_3)_3$), 31.29 ($-CH_2-$), 33.65 ($C(CH_3)_3$), 125.49, 127.72, 128.48, 128.59, 134.45, 143.49, 146.87, 147.02 (Ar), 174.29 (C=O) ppm.

### *5,11-Di-p-tert-butyl-17,23-bis(3-carboxypropyl)-25,26,27,28-tetrapentyloxycalix[4]arene* (**7**; $C_{64}H_{92}O_8$)

In 50 ml of dry *DMF*, 1 g (1.41 mmol) of **6** was dissolved; then, 0.17 g (4.23 mmol) of 60% NaH were added. After 30 min, 0.53 ml (4.23 mmol) of *n*-pentyl bromide was added, and the mixture was stirred at room temperature for 24 h. The next portion of NaH (0.17 g/4.23 mmol) and *n*-pentyl bromide (0.53 ml/4.23 mmol) was added, and the mixture was stirred again for 24 h. Finally, the third portion of NaH (1 g/25 mmol) and *n*-pentyl bromide (2 ml/16 mmol) was added, and the mixture was stirred for additional 5 days. After evaporation, 20 ml ethanol and 2 g NaOH were added, and the resulting suspension was refluxed for 3 h to hydrolyze the partially formed *n*-pentyl diester. The mixture was acidified with HCl to *pH* 2, solvents were evaporated, and chloroform (10 ml) and water (50 ml) were added. The organic layer was separated, and the aqueous phase was extracted with $CHCl_3$. The combined organic phases were washed twice with water, dried, and evaporated. After crystallization from EtOH/water, pure **6** was obtained as light yellow crystals.

Yield: 0.81g (58%); m.p.: 99–103°C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 0.95$ (t, $J = 7.98$ Hz, 6H, $CH_3$-), 0.98 (s, $J = 7.95$ Hz, 6H, $CH_3$-), 1.31 (s, 18H, $C(CH_3)_3$), 1.26 (m, 24H, $CH_2$), 1.86 (m, 4H, $CH_2CH_2CH_2$), 1.99 (t, $J = 6.9$ Hz, 4H, $ArCH_2CH_2CH_2$), 2.14 (t, $J = 7.5$ Hz, 4H, $ArCH_2CH_2CH_2$), 3.05 and 4.39 (2d, $J = 13.0$ Hz, 4H each, $ArCH_2Ar$), 3.67, (t, $J = 6.9$ Hz, 4H, $OCH_2$), 3.97 (t, $J = 7.0$ Hz, 4H, $OCH_2$), 6.09, (s, 4H, ArH), 7.03 (s, 4H, ArH) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 4.04$, 14.30, 22.7, 22.93, 25.75, 28.17, 28.60, 29.74, 30.16, 31.11, 33.71, 34.13 ($CH_2$), 31.57 ($C(CH_3)_3$), 33.95 ($C(CH_3)_3$), 74.95, 75.42 ($ArOCH_2$), 125.43, 127.05, 133.17, 134.00, 135.42, 144.44, 153.72, 154.90 (Ar), 180.09 (C=O) ppm.

### *5,11-Di-p-tert-butyl-17,23-bis(3-chloroformylpropyl)-25,26,27,28-tetrapentyloxycalix[4]arene* (**8**; $C_{64}H_{90}Cl_2O_6$)

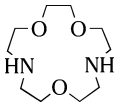
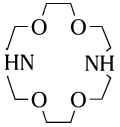
To a solution of 0.265 g (0.268 mmol) of **7** in 10 ml of dry $CH_2Cl_2$, 0.07 ml (0.8 mmol) of oxalyl chloride were added, and the mixture was refluxed for 1 h. After evaporation of the solvent and the excess oxalyl chloride, the residue was dried under vacuum for 3 h to give **7** in quantitative yield as a yellow foam which could not be recrystallized due to decomposition.

$^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 0.94$ (t, $J = 7.9$ Hz, 6H, $CH_3$-), 0.96 (s, $J = 7.95$ Hz, 6H, $CH_3$-), 1.32 (s, 18H, $C(CH_3)_3$), 1.23 (m, 24H, $CH_2$), 1.88 (m, 4H, $CH_2CH_2CH_2$), 1.99 (t, $J = 6.9$ Hz, 4H, $ArCH_2CH_2CH_2$), 2.12 (t, $J = 7.5$ Hz, 4H, $ArCH_2CH_2CH_2$), 3.05 and 4.39 (2d, $J = 12.9$ Hz, 4H each, $ArCH_2Ar$), 3.66 (t, $J = 6.9$ Hz, 4H, $OCH_2$), 3.99 (t, $J = 7.0$ Hz, 4H, $OCH_2$), 6.10 (s, 4H, ArH), 7.03 (s, 4H, ArH) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 14.03$, 14.32, 22.72, 22.95, 25.90, 28.15, 28.65, 29.80, 30.22, 31.20, 33.50, 34.89 ($CH_2$), 31.72 ($C(CH_3)_3$, 34.15 ($C(CH_3)_3$), 74.90, 75.41 ($ArOCH_2$), 125.63, 126.85, 132.93, 133.91, 135.54, 144.31, 153.61, 155.11 (Ar), 169.51 (C=O) ppm.

### *General procedure for the preparation of calix[4]amidocrowns* **9–12** *and calix[4]-amidocryptands* **13** *and* **14**

Solutions of diacid chloride **8** (0.268 mmol) and diamine (0.268 mmol), both in 10 ml of dry toluene, were simultaneously added dropwise to a vigorously stirred solution of triethylamine (0.11 ml,

**Table 1.** Yields, melting points, and characteristic spectroscopic data of compounds **9–14**

| | Diamine | Yield (%) | M.p. (°C) | $^1$H NMR (ppm) | | | | $^1$C NMR (ppm) | FD MS *m/z* ($M^+$) (calcd.) |
|---|---|---|---|---|---|---|---|---|---|
| | | | | ArH (s) | NH (br) | $ArCH_2Ar$ (ABq)[a] | *t*-Bu (s) | C=O (s) | |
| **9** | $H_2NCH_2CH_2OCH_2CH_2NH_2$ | 27 | 98–102 | 6.18<br>7.01 | 5.86 | 3.06<br>4.39 | 1.29 | 173.3 | 1057.1<br>(1057.53) |
| **10** | $H_2N(CH_2CH_2O)_2CH_2CH_2NH_2$ | 30 | 205–207 | 6.07<br>7.00 | 6.15 | 3.04<br>4.37 | 1.32 | 173.0 | 1101.5<br>(1101.58) |
| **11** | $H_2N(CH_2CH_2O)_3CH_2CH_2NH_2$ | 2.2 | 190–191 | 5.99<br>7.04 | 6.44 | 3.03<br>4.32 | 1.35 | 172.9 | 1145.5<br>(1145.64) |
| **12** | $H_2N(CH_2CH_2O)_4CH_2CH_2NH_2$ | 25 | 75–77 | 5.97<br>7.07 | 6.64 | 3.04<br>4.35 | 1.36 | 173.0 | 1189.6<br>(1189.66) |
| **13** |  | 25 | 194–197 | 6.04<br>7.12 | – | 3.04<br>4.37 | 1.38 | 172.9 | 1171.7<br>(1171.67) |
| **14** |  | 30 | 80–82 | 6.00<br>7.09 | –<br>– | 3.04<br>4.38 | 1.40 | 173.6 | 1215.7<br>(1215.72) |

[a] $J = 12.5–15.0$ Hz for ABq

0.8 mmol) in dry toluene (30 ml) during 6 h. The mixture was stirred overnight at room temperature, and the solvent was evaporated under reduced pressure. The resulting residue was purified by flash chromatography ($SiO_2$, $CH_2Cl_2$/MeOH = 95/5) to give a pure product. Yields, melting points, and characteristic spectroscopic data of calix[4]amidocrowns and calix[4]amidocryptands are summarized in Table 1.

*Calix[4]amidocrown* **9**[1] ($C_{68}H_{100}N_2O_7$)

Yield: 76 mg (27%); m.p.: 98–102°C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 0.91$ (m, 12H, $CH_3$), 1.22 (m, 24H, $CH_2$), 1.29 (s, 18H, $C(CH_3)_3$), 1.87 (m, 8H, $ArCH_2CH_2CH_2$), 2.09 (t, $J = 6$ Hz, 4H, $ArCH_2CH_2CH_2$), 3.06 and 4.39 (2d, $J = 13.4$ Hz, 4H each, $ArCH_2Ar$), 3.36 (t, $J = 5.5$ Hz, 4H, $CH_2CH_2O$), 3.50 (t, 4H, $CH_2CH_2O$), 3.69 (t, $J = 6.6$ Hz, 4H, $ArOCH_2$), 3.96 (t, $J = 8.7$ Hz, 4H, $ArOCH_2$), 5.86 (br, 2H, CONH), 6.18 (s, 4H, ArH), 7.01 (s, 4H, ArH) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 14.02$, 14.03, 22.69, 22.88, 26.44, 28.14, 28.54, 29.67, 30.11, 31.17, 33.88, 35.90 ($CH_2$), 31.63 ($C(CH_3)_3$), 33.96 ($C(CH_3)_3$), 39.18 ($NHCH_2CH_2O$), 69.67 ($CH_2O$), 74.95, 75.43 ($ArOCH_2$), 125.38, 127.01, 133.36, 134.09, 144.19, 153.80, 154.82, 155.18 (Ar), 173.34 (C=O) ppm; MS: $m/z = 1055.8$.

*Calix[4]amidocrown* **10** ($C_{70}H_{104}N_2O_8$)

Yield: 89 mg (30%); m.p.: 205–207°C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 0.91$ (m, 12H, $CH_3$), 1.25 (m, 24H, $CH_2$), 1.32 (s, 18H, $C(CH_3)_3$), 1.84 (m, 12H, $ArCH_2CH_2CH_2$), 3.04 and 4.37 (2d, $J = 12.9$ Hz, 4H each, $ArCH_2Ar$), 3.41 (t, $J = 5.1$ Hz, 4H, $CH_2CH_2O$), 3.52 (t, 4H, $CH_2CH_2O$), 3.60 (s, 4H, -$CH_2CH_2O$-), 3.68 (t, $J = 6.0$ Hz, 4H, $ArOCH_2$), 3.96 (t, $J = 8.3$ Hz, 4H, $ArOCH_2$), 6.07 (s, 4H, ArH), 6.15 (br, 2H, CONH), 7.00 (s, 4H, ArH) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz); $\delta = 14.03$, 14.28, 22.69, 22.91, 26.43, 28.15, 28.60, 29.71, 30.14, 31.15, 34.54, 36.63 ($CH_2$), 31.64 ($C(CH_3)_3$), 33.99 ($C(CH_3)_3$), 39.10 ($NHCH_2CH_2O$), 69.86, 70.27 ($CH_2O$), 74.93, 75.34 ($ArOCH_2$), 125.45, 126.93, 133.19, 134.16, 135.50, 144.15, 153.73, 154.93 (Ar), 173.03 (C=O) ppm; MS: $m/z = 1100.8$.

*Calix[4]amidocrown* **11** ($C_{72}H_{108}N_2O_9$)

Yield: 68 mg (22%); m.p.: 190–191°C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 0.90$ (m, 12H, $CH_3$), 1.20 (m, 24H, $CH_2$), 1.35 (s, 18H, $C(CH_3)_3$), 1.80 (m, 12H, $ArCH_2CH_2CH_2$), 3.03 and 4.32 (2d, $J = 13.1$ Hz, 4H each, $ArCH_2Ar$), 3.46 (t, $J = 5.0$ Hz, 4H, $CH_2CH_2O$), 3.52 (t, 4H, $CH_2CH_2O$), 3.62 (s, br, 8H, $CH_2CH_2O$), 3.65 (t, $J = 7.2$ Hz, 4H, $ArOCH_2$), 3.97 (t, $J = 8.8$ Hz, 4H, $ArOCH_2$), 5.99 (s, 4H, ArH), 6.44 (br, 2H, CONH), 7.04 (s, 4H, ArH) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta = 13.99$, 14.23 ($CH_3$), 22.66, 22.90, 26.52, 28.11, 28.61, 29.67, 30.15, 31.14, 34.57, 36.41 ($CH_2$), 31.65 ($C(CH_3)_3$), 34.00 ($C(CH_3)_3$), 39.02 ($NHCH_2CH_2O$), 70.04, 70.18, 70.48 ($CH_2O$), 74.83, 75.32 ($ArOCH_2$), 125.50, 126.85, 132.88, 135.73, 144.18, 153.61, 155.10, 155.18 (Ar), 172.94 (C=O) ppm; MS: $m/z = 1144.5$.

*Calix[4]amidocrown* **12** ($C_{74}H_{112}N_2O_{10}$)

Yield: 80 mg (25%); m.p.: 75–77°C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta = 0.90$ (m, 12H, $CH_3$), 1.20 (m, 24H, $CH_2$), 1.36 (s, 18H, $C(CH_3)_3$), 1.81 (m, 12H, $Ar(CH_2)_3$), 3.04 and 4.35 (2d, $J = 15.0$ Hz, 4H

[1] Systematic name: 27,36-Di-*tert*-butyl-22,32,40,42-tetrapentyloxy-11-oxa-8,14-diaza-hexacyclo[19.11.7$^{3,31}$.1$^{19,23}$.1$^{25,29}$.1$^{34.38}$]tritetraconta-1,3(41),19(43),20,22,25,27,29-(42),31,34,36,38(40)-dodecaen-7,15-dione

each, $ArCH_2Ar$), 3.41 (t, $J = 6.5$ Hz, 4H, $CH_2CH_2O$), 3.58 (t, 4H, $CH_2CH_2O$), 3.61 (m, 8H, $-CH_2CH_2O-$ and $ArOCH_2$), 3.94 (t, $J = 8.9$ Hz, 4H, $ArOCH_2$), 5.97 (s, 4H, ArH), 6.35 (br, 2H, CONH), 7.07 (s, 4H, ArH) ppm; $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta = 14.05$, 14.14 ($CH_3$), 22.67, 22.92, 26.87, 27.15, 28.11, 29.41, 29.90, 31.18, 34.65, 36.29 ($CH_2$), 31.57 ($C(CH_3)_3$), 34.03 ($C(CH_3)_3$), 39.04 ($NHCH_2CH_2O$), 69.77, 69.93, 70.37, 70.99 ($CH_2O$), 74.79, 75.25 ($ArOCH_2$), 125.38, 126.79, 127.06, 132.78, 135.86, 144.26, 153.58, 155.17 (Ar), 172.94 (C=O) ppm, MS: $m/z = 1187.6$.

*Calix[4]amidocryptand* **13** ($C_{74}H_{110}N_2O_9$)

Yield: 77 mg (25%); m.p.: 194–197°C, $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta = 0.91$ (t, $J = 7.3$ Hz, 12H, $CH_3$), 1.18 (m, 24H, $CH_2$), 1.38 (s, 18H, $C(CH_3)_3$), 1.79 (m, 8H, $ArCH_2CH_2CH_2$), 2.21 (t, $J = 6.9$ Hz, 4H, $ArCH_2CH_2CH_2$), 3.04 and 4.37 (2d, $J = 13.0$ Hz, 4H each, $ArCH_2Ar$), 3.33 (m, 24H, $CH_2CH_2O$ and $ArOCH_2$), 4.01 (t, $J = 8.4$ Hz, 4H, $ArOCH_2$), 6.04, (s, 4H, ArH), 7.12 (s, 4H, ArH) ppm; $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta = 13.97$, 14.29, 22.65, 22.93, 26.04, 28.10, 28.65, 29.84, 30.22, 31.12, 33.21, 34.08 ($CH_2$), 31.62 ($C(CH_3)_3$), 34.54 ($C(CH_3)_3$), 49.52, 50.52 ($CH_2N<$), 68.72, 69.31, 69.68 ($CH_2O$), 74.78, 75.42 ($ArOCH_2$), 125.54, 126.61, 132.51, 133.75, 135.95, 144.37, 153.23, 155.18 (Ar), 172.89 (C=O) ppm; MS: $m/z = 1169.7$.

*Calix[4]amidocryptand* **14** ($C_{76}H_{114}N_2O_{10}$)

Yield: 97 mg (30%); m.p.: 80–82°C; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta = 0.91$ (m, 12H, $CH_3$), 1.17 (m, 24H, $CH_2$), 1.40 (s, 18H, $C(CH_3)_3$), 1.80 (m, 4H, $ArCH_2CH_2CH_2$), 1.97 (t, $J = 7.5$ Hz, 4H, $ArCH_2CH_2CH_2$), 2.13 (t, $J = 8.4$ Hz, 4H, $ArCH_2CH_2CH_2$), 3.04 and 4.38 (2d, $J = 12.9$ Hz, 4H each, $ArCH_2Ar$), 3.49 (m, 28H, $CH_2CH_2O$ and $ArOCH_2$), 4.03 (t, $J = 7.3$ Hz, 4H, $ArOCH_2$), 6.00 (s, 4H, ArH), 7.09 (s, 4H, ArH) ppm; $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta = 14.02$, 14.34, 22.69, 22.95, 26.17, 28.12, 28.69, 29.65, 30.23, 31.23, 33.17, 35.02 ($CH_2$), 31.78 ($C(CH_3)_3$), 34.08 ($C(CH_3)_3$), 47.18, 49.25 ($CH_2N<$), 68.39, 69.59, 70.48, 71.00 ($CH_2O$), 74.78, 75.34 ($ArOCH_2$), 125.63, 126.82, 132.60, 133.89, 135.98, 144.17, 153.62, 155.29 (Ar), 173.60 (C=O) ppm; MS: $m/z = 1214.7$.

### *Membrane selectivity measurements*

#### *Chemicals*

All metal salts employed were of analytical grade and were purchased from POCh Gliwice, Poland. Standard solutions (0.1 *M*) of metal salts in redistilled water were prepared; working solutions were prepared as required by suitable dilution with redistilled water.

#### *Membranes materials*

High molecular weight poly(vinyl chloride) (PVC), potassium *tetrakis*(*p*-chlorophenyl) borate (*KTpClPB*), and didecyl phthalate (*DDP*) were obtained from Fluka, Buchs, Switzerland. As solvent for membrane components freshly distilled tetrahydrofuran (*THF*) p.a. (POCh Gliwice) was used.

#### *Membrane and electrode preparation*

The membrane components (1% (w/w) of ionophore, 50% mol of *KTpClPB* (with respect to the ionophore), 30% (w/w) of PVC, and 68–69% (w/w) *DDP* as plasticizer), totalling 100 mg, were dissolved in 1.5 ml of freshly distilled *THF*. This solution was poured into 24 mm i.d. glass rings resting on a glass plate. After solvent evaporation overnight, the resulting membrane was peeled off from the glass mold, and disks of 7 mm diameter were cut out. The membrane disks were mounted in

electrode bodies (type IS 561, Philips, Eindhoven, Netherlands) for EMF measurements. The electrode was left overnight in conditioning solutions of NaCl or LiCl. Two electrodes were prepared for each composition of membrane.

*EMF measurements*

All measurements were carried out at 20°C with cells of the type Ag,AgCl;$KCl_{(satd)}$ 0.1 *M* $KNO_3$/ sample//membrane//internal filling solution;AgCl;Ag. A solution of sodium or lithium chloride at fixed *pH* was used as internal filling solution. The potentials were recorded by a customer made 16-channel electrode monitor (resolution 200 μV) equipped with one FET operational amplifier per channel (input impedance $10^{12}\,\Omega/2$ pF). The data acquisition was performed with a PC and own software [18].

The potentiometric selectivity coefficients, $K^{pot}_{Na,M}$ were determined by the SSM method (separate solution method) [19], measuring potentials in $10^{-2}$ *M* solutions of the metal chlorides at constant $pH = 6$. EMF values of the electrodes were measured in each solution for 10 min at intervals of 30 sec. An average of the last five measurements was taken to further calculations.

## Acknowledgements

This work was supported by the *Polish State Committee for Scientific Research* within the grant No 3T09A14810 (PB075/T09/96/10) and in part by the *International Bureau of the BMBF* (grant NO POL-191-96) within German-Polish Cooperation.

## References

[1] Böhmer V (1995) Angew Chem **107**: 785 (1995) Angew Chem Int Ed Engl **34**: 713
[2] Arnaud-Neu F, Schwing-Weill M-J (1997) Synth Metals **90**: 157
[3] (a) Ulrich G, Ziessel R, Manet I, Guardigli M, Sabbatini N, Fraternali F, Wipff G (1997) Chem Eur J **3**: 1815; (b) Abidi R, Harrowfield JM, Skeleton W, White AH, Asfari Z, Vincens J (1997) J Incl Phenom Mol Recogn **27**: 291; (c) Ulrich G, Turek P, Ziessel R (1996) Tetrahedron Lett **37**: 8755; (d) Regnouf-de-Vains J-B, Lamartine R (1996) Tetrahedron Lett **37**: 6311
[4] (a) Ghidini E, Ugozzoli F, Ungaro R, Harkema S, El-Fadl AA, Reinhoudt DN (1990) J Am Chem Soc **112**: 6979; (b) Brzózka Z, Lammerink B, Ghidini E, Ungaro R, Reinhoudt DN (1993) J Chem Soc Perkin Trans 2, 1037
[5] (a) Reinhoudt DN, Dijkstra PJ, Veld in't PJA, Bugge KE, Harkema S, Ungaro R, Ghidini E (1987) J Am Chem Soc **109**: 4761; (b) Dijkstra PJ, Burnink JAJ, Bugge K-E, Reinhoudt DN, Harkema S, Ungaro R, Ugozzoli F, Ghidini E (1989) ibid **111**: 7567
[6] Casnati A, Pochini A, Ungaro R, Ugozzoli F, Arnaud F, Fanni S, Schwing M-J, Egberink RJM, de Jong F, Reinhoudt DN (1995) J Am Chem Soc **117**: 2767
[7] Ostaszewski R, Stevens TW, Verboom W, Reinhoudt DN, Kaspersen FM (1991) Rec Trav Chim Pays-Bas **110**: 294
[8] Arnaud-Neu F, Böhmer V, Dozol J-F, Grüttner C, Jakobi RA, Kraft D, Mauprivez O, Rouquette H, Schwing-Weill M-J, Simon N, Vogt W (1996) J Chem Soc Perkin Trans 2, 1175
[9] (a) Harrowfield JM, Ogden MI, Richmond WR, White AH (1991) J Chem Soc Chem Commun 1159; (b) for solutions studies see Assmus R, Böhmer V, Harrowfield JM, Ogden MI, Richmond WR, Skelton BW, White AH (1993) J Chem Soc Dalton Trans 2427
[10] van Loon J-D, Groenen LD, Wijmenga SS, Verboom W, Reinhoudt DN (1991) J Am Chem Soc **113**: 2378
[11] Paek K, Ihm H (1996) Chem Lett 311
[12] Ihm H, Kim K, Paek KJ (1997) J Chem Soc Perkin Trans 1, 1997

[13] (a) Ostaszewski R, Stevens TW, Verboom W, Reinhoudt DN, Kaspersen FM (1991) Rec Trav Chim Pays-Bas **110**: 294; (b) Böhmer V, Ferguson G, Gallagher JF, Lough AJ, McKervey MA, Madigan E, Moran MB, Phillips J, Williams G (1993) J Chem Soc Perkin Trans 1, 1521
[14] Gutsche CD, Iqbal M (1990) Org Synth **86**: 234
[15] See KA, Fronczek FR, Watson WH, Kashyap RP, Gutsche CD (1991) J Org Chem **56**: 7256
[16] Still WC, Kahn M, Mitra A (1978) J Org Chem **43**: 1923
[17] Martin EL (1922) J Am Chem Soc **58**: 1440
[18] Brzozka Z (1988) Pomiary Automatyka Kontrola **5**: 422
[19] Lewenstam A, Hulanicki A (1990) Selective Electrode Rev **12**: 161

*Received May 20, 1998. Accepted June 5, 1998*