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New water-soluble calix[4]arene-bis(benzocrown-6) for caesium–sodium separation by nanofiltration–complexation

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Abstract—Calix-bis(benzocrown-6) **6** and **7** were converted into the water-soluble receptors **9**, **10**, **12** and **15** by introducing hydroxy, carboxy, sulfato or diethanolamino groups at the *para* position of the phenolic ring and/or on the benzo-ether moieties. The complexation properties of these ionophores were studied for all alkali cations in methanolic and aqueous media. Stability constants were calculated by UV–Vis spectroscopy. All ligands showed a more or less affinity for the larger cations, depending on the nature and the position of the substituents grafted on the benzo-ether chain only or both on the calixarene ring and the benzo-ether loop. For selective Cs^+/Na^+ separation, the efficiency of the ligands was evaluated by means of a nanofiltration system. In comparison with the known tetrahydroxylated bis-crown-6 calix[4]arene **1**, compounds **9**, **12** and **15** represent the most selective ligands for the Cs^+ cation in a moderate salted medium ($[NaNO_3]$=85 g/L).
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1. Introduction

Due to their interesting selective binding abilities towards alkali cations, calixcrowns[1] constitute an important class of macrocyclic compounds combining calixarene[2] and crown ether[3] frameworks. Particularly important are the dialkoxycalix[4]arene(crown-6) derivatives[4–14] and analogous bis-(crown-6)[15–19] in 1,3-alternate conformation which showed in many cases a high selectivity towards caesium ions. Thus numerous studies concerning solvent extraction[6,20] or liquid membrane transport,[18] solution thermodynamics,[6,10] detection,[21,22] X-ray crystal structure and molecular modeling[8,23–29] have been performed on these receptors. This has opened up new possibilities for radioactive ^{137}Cs separation from nuclear fuel reprocessing solutions containing much larger amounts of sodium[30] (20×10^3 times as much than caesium) which have become of crucial interest for the nuclear industry.

Since becoming involved in this project, we chose to use the technique of nanofiltration–complexation (NF) as a membrane separation process,[31,32] especially dedicated to the basic effluents reprocessing, resulting from the nuclear facilities washing.

Nanofiltration techniques showed great potential for the separation of metal cations in aqueous phase. It allowed the separation of different ion valences, but selectivity was not generally ensured for the separation of ions with same valences. This could be improved by associating the nanofiltration step to a preliminary selective complexation step with water-soluble ligands of molecular weight higher than the 'cut off' of the membrane (300–1000 g mol). In previous reports we described the synthesis and the evaluation of several water-soluble calix[4]arene-bis-(crown-6)[33,34] incorporating neutral or proton-ionizable substituents such as sulfonamide, sulfonate, carboxy and hydroxy groups at the *para* position of the aromatic ring. The selective complexation of caesium towards alkali ions (Na^+, K^+, Rb^+, Cs^+) and with these ligands were studied in basic aqueous media by UV–Vis analysis, NMR spectroscopy and nanofiltration–complexation tests.[35] Some of these ligands showed a more or less pronounced affinity for the target ion. In fact, these studies allowed us to prove that the efficiency of these macrocycles depended on the number and the nature of the grafted hydrophilic functionalities. These play a major role in the complexation and stabilization of the caesium ion both in the cavity of the hydrophobic aromatic ringligand and in the crown ether chain as also described by Vicens et al.[36] with *para*-sulfonated 1,2;3,4-calix[4]arene-bis(crowns) in the 1,2-alternate conformation or by Bartsch et al.[37,38] in a liquid–liquid extraction process with different calixcrowns mono-substituted. With a Cs^+/Na^+ selectivity of 6570, the

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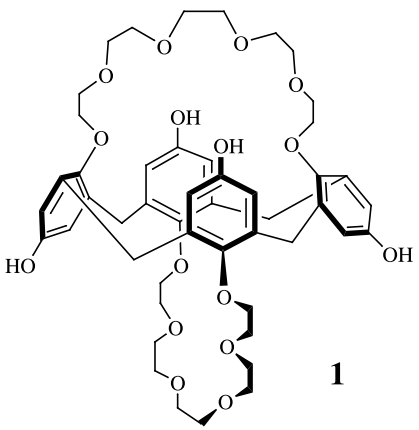


Figure 1. 5,11,17,23-Tetrahydroxycalix[4]arene-bis(crown-6).

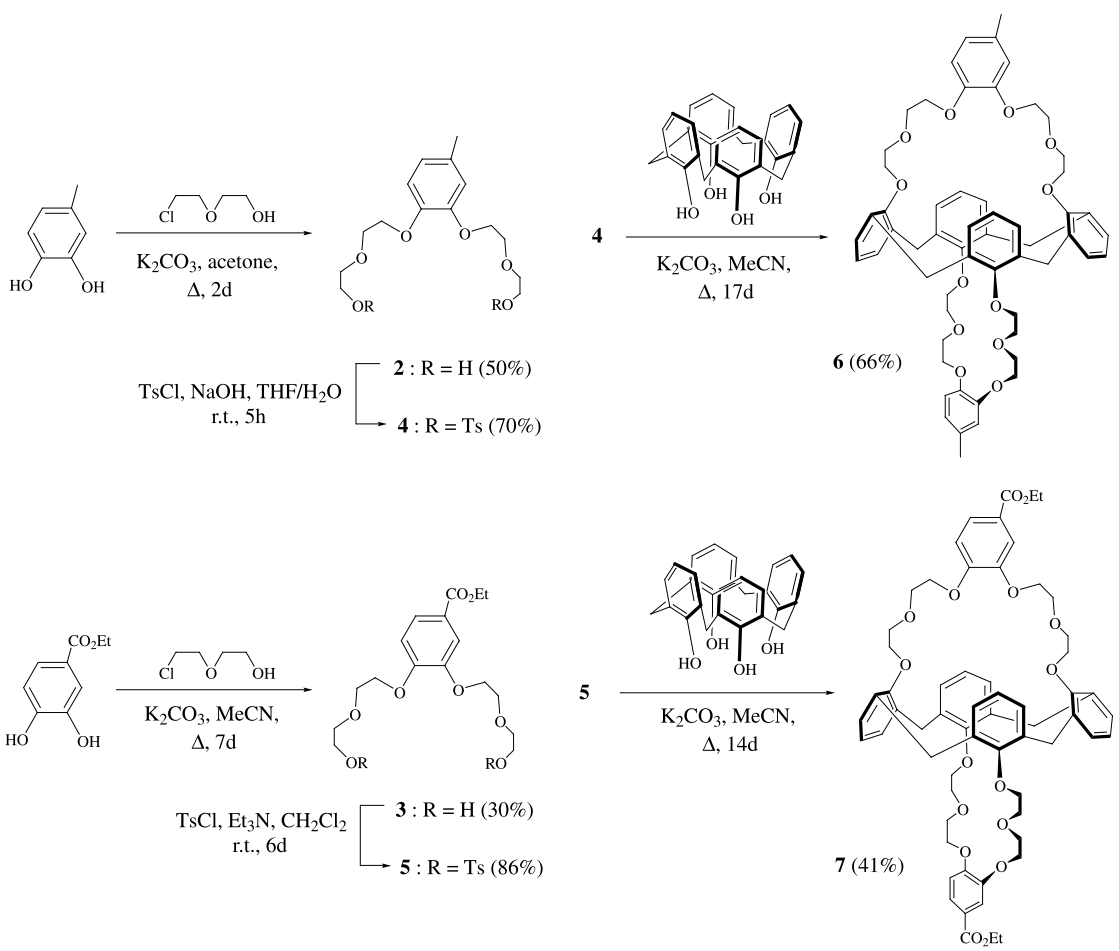
5,11,17,23-tetrahydroxycalix[4]arene-bis(crown-6) **1** (Fig. 1) was the best receptor for the caesium.[35] This achieved the best compromise between preorganization, steric hindrance and cooperative effect of the cation–arene and cation–phenolate interactions. Nevertheless, we estimated that the Cs^+/Na^+ selectivity could be enhanced using water-soluble calix[4]arene-bis(benzo-crown-6) of which lipophilic analogues exhibited better selectivities in organic medium.[18,39–43]

We report in this paper the synthesis of several new water-soluble benzo-crown-6 derivatives of calix[4]arene, a study of their affinity towards Cs^+, Rb^+, K^+ and Na^+ cations in methanol and in aqueous media, and finally the various aspects of the use of these ligands in a nanofiltration–complexation process. The water-soluble macrocycles were obtained by the preliminary preparation of two new lipophilic calixcrowns, the calix[4]arene-bis-[(4-methyl-1,2-phenylene)crown-6] **6** and the bis-[(4-ethoxycarbonyl-1,2-phenylene)crown-6] analogue **7**. These macrobicycle ligands were characterised by the presence of a calixarene ring and two substituted catechol subunits which could be modified separately or together. Thus, water-soluble derivatives were obtained either by modifying the ester function of **7** or by the incorporation of hydrophilic groups on the methyl-phenylene moiety and the calixarene ring of **6** at once.

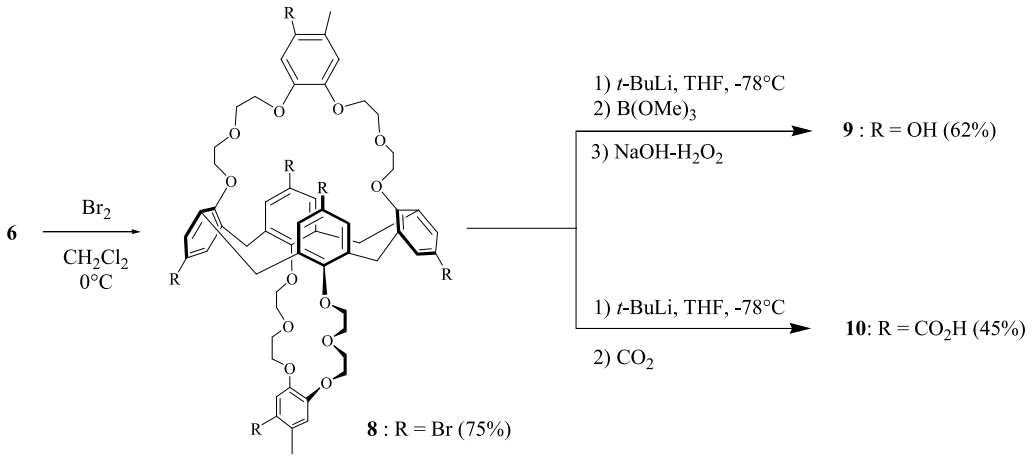
2. Results and discussion

2.1. Synthesis and characterisation

Calix[4]arenes bis(crown-6) **6** and **7** were synthesized according to the established method of Vicens et al.[18,44] They were obtained as a mixture of two enantiomers (Scheme 1). 4-Methyl-catechol and ethyl-3,4-dihydroxybenzoate were reacted with 2-(2-chloroethoxy)ethanol in the presence of K_2CO_3[45,44] to give the diols **2** and **3** in



Scheme 1.



Scheme 2.

acceptable yields. Ditosylates **4** and **5** were respectively obtained in good yields by reaction of tosylchloride with **2** and NaOH in THF–H_2O or **3** in CH_2Cl_2 and Et_3N. Finally, macrocyclisation with the calix[4]arene and ditosylates **4** and **5** were performed in refluxing CH_3CN in the presence of K_2CO_3 to give calixcrowns **6** and **7** with respectively 66 and 41% yields. Symmetrical 1,3-alternate structures of these compounds were determinated by NMR spectroscopy which showed very simple patterns. Thus, derivatives **6** and **7** exhibited well defined ^{1}H NMR spectra. The 1,3-alternate conformations were deduced from the presence of one singlet at 3.78 ppm for **6** and 3.76 ppm for **7** corresponding to the resonance signals of the Ar*CH*$_2$Ar protons. ^{13}C NMR spectroscopy confirmed these structures,[46] since only one signal assigned to the bridging methylene carbons was present at 37.92 ppm for **6** and 37.78 ppm for **7**.

Water-soluble derivatives **9** and **10** were obtained in two steps as depicted in Scheme 2. Subsequent bromination of **6** with Br_2 in CH_2Cl_2 at 0°C afforded the hexa-bromo derivative **8** (75%). Treatment of compound **8** with an excess of *t*-BuLi in dry THF at −78°C for 90 min followed by quenching with $B(OMe)_3$, oxidation with 3 M NaOH–35% H_2O_2 or quenching with CO_2 gave polyol **9** and polyacid **10** in 62 and 76% yield, respectively.

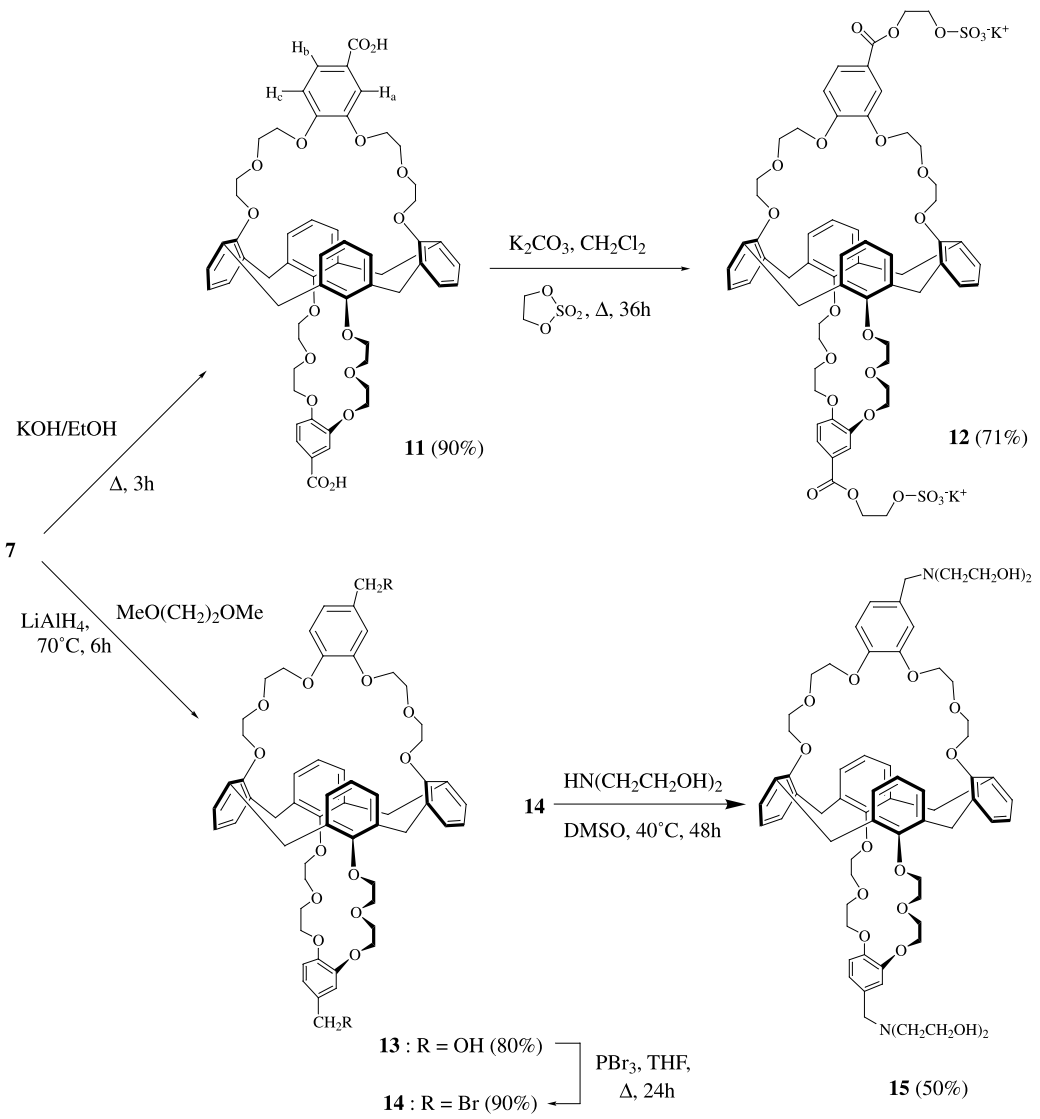
Exhaustive substitution of **6** in the fixed 1,3-alternate cone conformation simplified the characterisation of the reaction products by NMR in CD_3Cl. One singlet for the Ar*H meta* of the calixarene ring, two singlets for the residual Ar*H* of the benzo(crown) moiety and one singlet for the bridged methylene allowed the characterisation of each macrocyclic frame by ^{1}H NMR.

Modification of the ester groups of derivative **7** afforded ligands **12** and **15** soluble in water at pH 7, in two and three steps (Scheme 3). The synthesis of disulfato derivative **12** involved the hydrolysis of the ester group with KOH in refluxing ethanol followed by the reaction of the carboxylic acid intermediate **11** with 1,2,3-dioxathiolane-2,2-dioxyde in the presence of K_2CO_3 in CH_2Cl_2 to give **12** in an overall yield of 64%. Compound **15** was obtained via the synthesis of dibromomethyl intermediate **14**. In order to prepare the latter, radical bromination of ligand **6** was attempted under the usual conditions (NBS, benzoyl peroxide or AIBN in CCl_4) but these synthetic routes failed. Vicens et al.[1] synthesised a dibromomethyl analogue by the reduction of calix[4]arene1,3;2,4-bis-[(5-ethoxycarbonyl-1,3-phenylene)crown-6] with 40 equiv. of $LiAlH_4$ in Et_2O followed by the conversion of the diol into the dibromomethyl derivative with an excess of PBr_3 in Et_2O. By using the same procedure, reduction of **7** gave dihydroxymethyl **13** in a low yield of 10% even though the reaction time was extended to 5 days. On the other hand, when 1,2-dimethoxyethane was used instead of Et_2O, **13** was obtained in 80% yield. Treatment of diol with PBr_3 in THF afforded **14** in 90% yield which was finally converted into the bis-diethanolamine **15** with $HN(CH_2CH_2OH)_2$ in DMSO in 50% yield. In the case of compound **12**, ^{1}H NMR (Fig. 2) showed that the aromatic signals of the calixarene ring were slightly different to those expected (spectrum A). Indeed, calixarene protons were characterised by two overlapped triplets at 6.57 and 6.59 ppm (H_a, $H_{a'}$) and two overlapped doublets at 7.11 and 7.13 ppm (H_b, $H_{b'}$) demonstrating an unexpected dissymmetry of the structure of the receptor. This anomaly disappeared when a drop of DCl (spectrum B) was added in the NMR sample and phenolic protons of the calixarene ring were characterised by a triplet at 6.53 ppm and a doublet at 7.09 ppm. This phenomenon could be explained by the possible complexation of one of the potassium ion of the sulfonate chain which could be trapped inside the corresponding crown ether chain. Furthermore, the presence of well defined signals indicated a rapid cation–crown ether exchange between both sulfonates substituents.

Due to their structural analogy, calixcrowns derivatives **11**, **13**–**15** were characterised by similar ^{1}H and ^{13}C NMR resonance signals in CD_3Cl (**14**) or DMSO-d_6 (**11**, **13**, **15**) corresponding to the Ar*CH*, Ar*C*, Ar*CH*$_2$Ar and O*CH*$_2$*CH*$_2$O protons and carbons.

The removal of the triplet and the quadruplet of ethyl ester protons of **7** in the ^{1}H NMR spectra and the presence of signals assigned to the grafted substituents confirmed the modification of the benzo ether chains (COO*H* of **11** appeared at 12.71 ppm and benzylic *CH*$_2$ of **13**, **14** and **15** at 4.43, 4.52 and 3.64 ppm, respectively).

Mass measurements, performed by electrospray technique



Scheme 3.

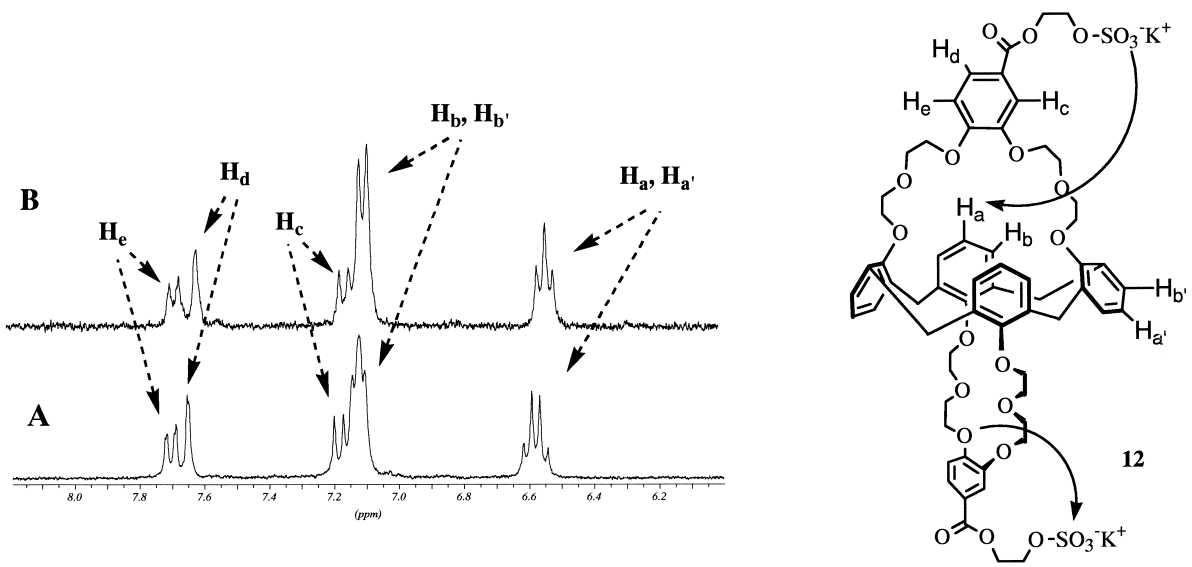


Figure 2. ^{1}H NMR of compound **18** (A: in DMSO-d_6, B: in DMSO-d_6+DCl).

Table 1. Determination of Cs or Na-ligands **9**, **10**, **11**, **15** complexes association constants by UV spectrometry in methanol

Ligand	**1**[35]	**9**	**10**	**11**	**15**
log β'_{Cs-L}	5.79±0.01	5.89±0.01	5.44±0.01	5.81±0.01	5.80±0.01
log β'_{Na-L}	3.5±0.2	3.2±0.2	3.3±0.2	2.9±0.3	3.0±0.3

were in accordance with the hosts' expected structures, particularly the mass spectrum of the dipotassium salt **12** which showed two signals at *m/z* 1359.2 and 1375.2 corresponding to the monocharged species ([**12**+Na]$^+$ and [**12**+K]$^+$).

2.2. Complexation studies

2.2.1. UV–Vis studies. The molecular recognition properties of the hydrophilic calix[4]arene-bis(benzocrowns) compounds **9**–**12** and **15** towards alkali ions were studied by UV–Vis spectroscopy analysis and compared with the complexation properties of the macrocycle **1**, in methanol and/or in basic aqueous medium depending on the solubility of ligands. The association constants β of the metal–ligand complexes were determined by absorption method, in which β is a constant ratio ([ML$^+$]/[M$^+$][L]) corresponding to the equilibrium M$^+$+L↔ML (M$^+$ is Na$^+$, K$^+$, Rb$^+$ or Cs$^+$ and L is the ligand). The absorption changes in the UV spectra of the ligand were recorded as alkali ions were progressively added to the medium containing a fixed amount of receptor. These modifications allowed the calculation of β_{ML} stability constants, according to the Foster–Hammick–Wardley method.[47]

2.2.2. Methanolic medium. Ligands **9**, **10**, **11** and **15** were tested by UV–Vis analysis in methanol toward Cs$^+$ and Na$^+$ cations and recorded between 240 and 330 nm. Addition of CsCl to the ligands solution induced bathochromic effects, whereas NaCl additions induced hypsochromic effects on the band of each ligand at 285±3 nm and in some cases, the appearance of isobestic points. For every ligand, a 1:1 M$^+$–ligand ratio was deduced from the straight line corresponding to the plot of Δ_{abs}/[MCl] versus Δabs which allowed the calculation of the association constant β from the slope. Association constants without units, $\beta'=\beta\rho_{MeOH}$ are given in Table 1. As a general rule, the introduction of benzo groups in the crown loop leads to a decrease in the stability of the Na$^+$–ligand complexes while no change was observed in the stability of Cs$^+$–**11** and Cs$^+$–**15** complexes as already mentioned by Arnaud-Neu et al.[48] with the calix[4]arene-dibenzo(crown-6). On the other hand, the stability of the Cs$^+$–**9** complex was enhanced, certainly due to the good compromise between the rigidification of the crown part and the cooperative effect of the cation–arene and cation–OH interactions. The stability of the Cs$^+$–**10** complex was lower due to the likely steric hindrance generated by the presence of the four carboxy groups grafted on the calixarene part. Finally, the presence of ionizable substituents on the phenolic ring seemed to increase the stability of Na$^+$–ligand with $\beta'_{Na/1}$, $\beta'_{Na/9}$ and $\beta'_{Na/10}$ values higher than those obtained with unsubstituted derivatives **11** and **15**.

2.2.3. Aqueous medium. The complexing ability of water-soluble ligands **9**, **10**, **12** and **15** toward Cs$^+$, Rb$^+$ and K$^+$ ions was also studied in aqueous medium in the same conditions. The association constants given in Table 2 are apparent constants β^*, because they depend on Na$^+$ amounts in the medium. Meanwhile the complexing ability of calixarenes toward other alkali ions such as Cs$^+$, Rb$^+$ and K$^+$ could be estimated. Carboxyl derivative **10** induced a hypochromic effect of the absorption band at 246 nm owing to the interaction of ligands with caesium and rubidium cations. The presence of only one isobestic point at 278 nm confirmed the 1:1 Cs$^+$–**10** ratio, as well as the straight line corresponding to the plot of Δ_{abs}/[MCl] versus Δ_{abs} in accordance with the Foster–Hammick–Wardley procedure (Fig. 3).

Table 2. Logarithms of the apparent association constants (log $\beta^*\pm\sigma_{n-1}$) of alkali–ligand complexes by UV spectrometry for ligands **9**, **10**, **12** and **15** in aqueous medium at 20°C (standard deviation σ obtained from n experiments with $2<n<4$)

Ligands	**1**[35]	**9**	**10**	**12**	**15**
[NaOH] (mol/L)	0.01	0.01	0.001	0.01	0.01
λ_{max} (nm)	304	305	246	284	286
Cs$^+$	5.63±0.01	5.75±0.01	5.38±0.01	5.71±0.01	5.70±0.01
Rb$^+$	5.27±0.02	5.34±0.02	4.78±0.04	5.37±0.02	5.36±0.02
K$^+$	4.60±0.06	4.50±0.06	N.d.	4.35±0.06	4.34±0.06

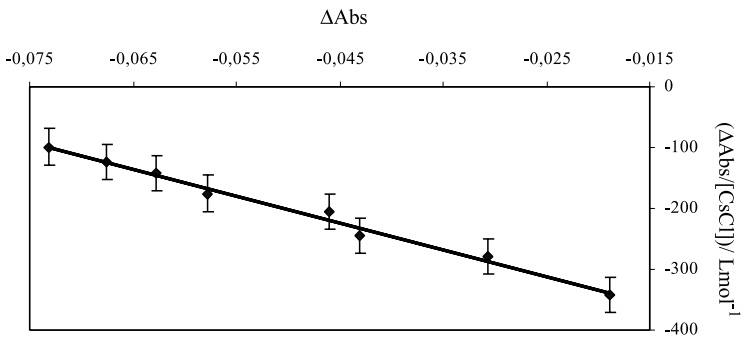


Figure 3. Plot of Δ_{abs}/[CsCl]=$f(\Delta_{abs})$ with ligand **10** in NaOH 0.1 M at room temperature.

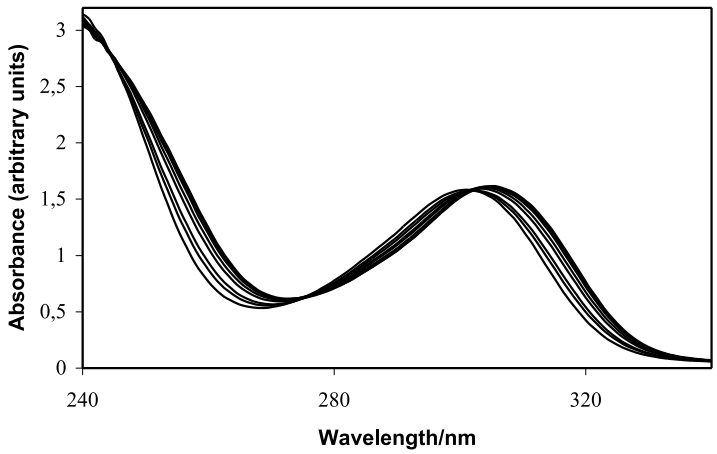


Figure 4. Changes in the absorption spectrum of a solution of ligand **9** with CsCl addition in water ([**9**]=2×10^{-4}mol/L; pH=12.5).

Interactions of CsCl with compound **9** resulted in significant hyperchromic and bathochromic shifts. Variations of absorption resulted in three isobestic points at 245, 275 and 302 nm (Fig. 4) and the straight line from the plot of Δ_{abs}/[MCl] versus Δ_{abs} proved the formation of 1:1 complexes with Cs^+. Finally, the spectra of solutions of ligands **12** and **15** containing increasing amount of CsCl and RbCl present the same pattern. The addition of metal ion induced an increase of the intensity of the two main absorption bands of each ligand (252 and 284 nm) with a low bathochromic shift and the appearance of two isobestic points at 248 and 265 nm for **12** and 245 and 260 nm for **15**. With K^+, **9**, **12** and **15** showed a moderate affinity (log β^*_{K-L}=4.50, 4.35, 4.34, respectively). As observed in methanol, the addition of **9** with four hydroxyl side arms on the calixarene ring or **12** and **15** with no substituents on it exhibited much higher complexation efficiency towards metal cations (log β^*_{Cs-L}=5.75, 5.71, 5.70 and log β^*_{Rb-L}=5.34, 5.37, 5.36, respectively) than **10** with carboxy substituents (log $\beta^*_{Cs-\mathbf{10}}$=5.38, log $\beta^*_{Rb-\mathbf{10}}$=4.78). Finally, the complexation level of Cs^+ by calixcrowns **1**, **12**, **15** was practically the same and lower than the one obtained with **9**.

Results confirmed that the efficiency of the ligand involved a good synergy between the nature of the polyether chain and the number and the nature of the substituents grafted on the phenolic ring. In both solvents, the selectivity increase according to the sequence **10**<**1**<**12**=**15**<**9**. On the other hand, the presence of the aryl group in the polyether chain and the OH function resulted in a polar and rigid macrocyclic cavity enough to maximise the cation–ligand interactions in basic aqueous media with a higher selectivity for the polyhydroxy derivative **9**.

2.2.4. NMR study. The ability of the receptors **9**–**12** and **15** to complex with Na^+ and Cs^+ was also studied by the use of ^{1}H NMR spectroscopy in DMSO-d_6. Addition of $NaNO_3$ in excess to solutions of ligands showed that no complexation of Na^+ occurred in view of the insignificant changes from the free ligands spectra observed. On the other hand, addition of $CsNO_3$ in excess to solutions of ligands led to appreciable changes due to the proximity of the Cs^+ cation nearby the altered protons. Thus, due to the π–Cs^+ interactions,[48] downfield shifts of the aromatic proton's resonance of the phenolic rings were observed (Table 3) and were characterised by relatively sharp signals. Similarly, the changes in the level of the signals of the protons of the glycolic chains were also indicative of the interaction of Cs^+ with oxygen donor atoms. As an example, the low downfield shift of the *meta* phenolic protons' resonance of **10** (Δ_δ=0.03 ppm) and the higher one corresponding to the multiplet of the OCH_2CH_2OPh ($\Delta\delta$=0.23 ppm) could be interpreted by weak π–aromatic interactions which let suppose the presence of an *exo* complex with the cation located within the polyether loop and stabilized by the COOH groups. A second example showed that the addition of $CsNO_3$ in excess to a solution of **11** was accompanied by downfield shifts of the triplet and doublet assigned to the *para* and *meta* phenolic protons ($\Delta\delta$=0.07 and 0.16 ppm, respectively) suggesting the presence of an *endo* complex. Similar effects were observed with ligands **15** and **12**.

Furthermore, to confirm the 1:1 stoichiometry of the Cs^+ complexes, a ^{1}H NMR study was also performed with the 1:1 complex of L–Cs^+NO_3 at room temperature. In comparison of the spectral modifications obtained upon the addition of $CsNO_3$ in excess, no significant changes were observed with a ratio ligand/caesium of 1:1, assuming the 1:1 stoichiometry for the cation complex in polar solvent as predicted by Wipff.[25] For all ligands, the presence of only one singlet for **9** and **10** or one triplet and one doublet for **11** and **15** corresponding to the signals of the phenolic protons seemed to indicate either a rapid cation–ligand exchange or

Table 3. Changes in the ^{1}H NMR aromatic shifts of **9**–**12** and **15** upon addition of $CsNO_3$ in DMSO-d_6

Compound	**9**	**9**⊂Cs^+	**10**	**10**⊂Cs^+	**11**	**11**⊂Cs^+	**12**	**12**⊂Cs^+	**15**	**15**⊂Cs^+
H in *meta*	6.40	6.64	7.76	7.79	7.03	7.19	7.11–7.13	7.19	6.99	7.10
H in *para*	–	–	–	–	6.58	6.64	6.57–6.59	6.67	6.58	6.67

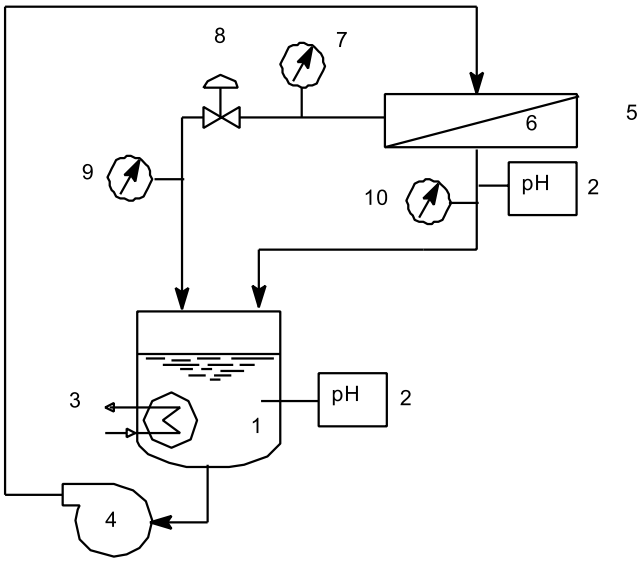


Figure 5. Schematic flow diagram of the lab-scale membrane system, 1: feed tank, 2: pH meter, 3: heat exchanger, 4: pump, 5: cell body, 6: membrane, 7: feed pressure gauge, 8: feed flow control valve, 9: retentate flux meter and 10: permeate flux meter.

a symmetrical position in the aromatic ring of the ligand, as suggested by Arnaud-Neu et al.[48] for the calix[4]arene-bis-crown-6-Cs^+I^- complex studied in deuterated acetonitrile.

2.2.5. Caesium–sodium separation by nanofiltration–complexation. The water-soluble calixcrown derivatives were subsequently used as specific ligands for caesium in a nanofiltration–complexation process. Nanofiltration–complexation tests were carried out to measure the ligand ability in order to help improve the separation of caesium from sodium by the nanofiltration process. In the range of 300–1000 g/mol molecular weights, nanofiltration membrane 'cut offs' are located between ultrafiltration and reverse osmosis. Nanomax 50 membrane allowed only 10% retention of Na^+ and Cs^+ ions. Then selective complexation of caesium with a ligand of larger size and mass than the target should increase the retention of this latter preventing this ion from passing through the membrane. A schematic representation of the nanofiltration (NF) loop used in our experiments is given in Figure 5. By totally recycling the permeate and the retentate, the feed remains at constant composition during the experiment.

First, the selective caesium affinity of ligands was studied in an aqueous medium (400 mL) containing low levels of sodium nitrate. Several known amounts of a selected ligand were progressively added to a solution containing fixed concentrations of caesium (15 mg/L) and sodium nitrates (0.1 mol/L) which was filtered on a NF membrane. Samples of permeate and retentate were taken half an hour after each ligand addition.

Table 4. Experimental conditions of the solubility (pH and the temperature) of **9**, **10**, **11**, **15** in a solution of $NaNO_3$ (50 mL, 0.1 M)

Ligands	**1**[35]	**9**	**10**	**12**	**15**
[L] (g/L)	4.03	4.73	5.50	6.00	5.23
pH	12	12.5	11	7	7
T (K)	298	298	298	303	303

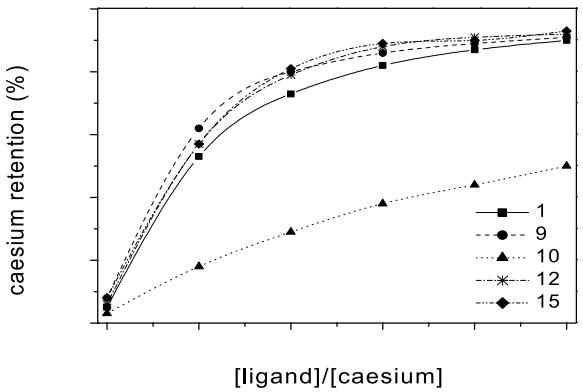


Figure 6. Caesium retention=*f*([ligand]/[caesium]) ([caesium=15 mg/L, $[NaNO_3]$=0.1 mol/L, *T*=293 K, ΔP=0.06 MPa).

Nanofiltration–complexation experiments were also performed in the conditions of the solubility of each ligand. This solubility was determined for each receptor before testing them in the nanofiltration–complexation process. Thus, water-soluble ligands **9**, **10**, **12** and **15** were preliminary dissolved in a 0.1 M sodium nitrate solution (50 mL) in the conditions of pH and temperature ensuring a total solubility of the quantity of the ligands, required to reach a ratio [ligand]/[caesium] of **5** (Table 4).

In the absence of ligand, the performances of the nanofiltration membrane used (Nanomax 50 membrane) were not really affected by the experimental conditions (pH and temperature) and were not sufficient (Fig. 6). With a ratio [ligand]/[caesium] equal to 5, caesium retention was respectively of 91, 92 and 93% for hydrosoluble derivatives **9**, **12** and **15** which showed a good affinity toward caesium as well as the compound **1**. These were much higher than with carboxylic analogue **10** of which retention rates varied identically until 50% with a [ligand]/[caesium] molar ratio of 5.

Since the purpose of this work was to improve the separation of traces of caesium contained in high concentrated sodium salt media, a second experiment was performed to evaluate and to compare the Cs^+/Na^+ selectivity of the ligands by addition of known amounts of sodium nitrate to a solution

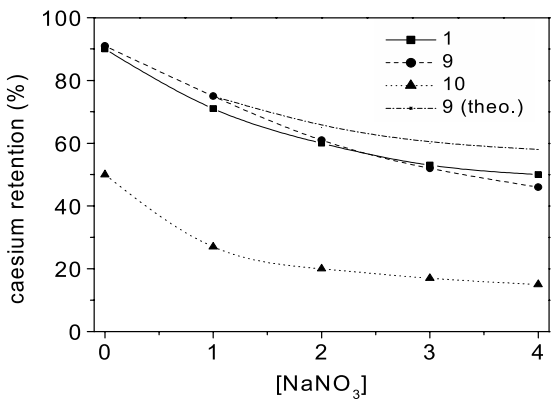


Figure 7. Caesium retention=*f*($[NaNO_3]$) ([caesium=15 mg/L, [ligand]/[caesium]=5, *T*=293 K, ΔP=0.06 MPa).

containing a fixed ratio [ligand]/[caesium] of 5, which was then filtered on the NF membrane.

When $NaNO_3$ was added, the Cs^+/Na^+ selectivity of ligands **9**, **12** and **15** decreased (Fig. 7). In fact, in a 1 mol/L $NaNO_3$ basic aqueous medium with a ratio [ligand]/[caesium] of 5, the caesium retention by the NF membrane was still close to 80%. Surprisingly, when the sodium nitrate concentration varied from 1 to 4 mol/L, the experimental Cs^+/Na^+ selectivity of these ligands decreased abnormally. Although the tests were performed in closed loop and the caesium measuring out should remain constant in the retentate, an unusual decrease of the caesium concentration in the retentate was noticed. Thus, with absorption values theoretically constant in the retentate, caesium retention should rise to 76, 65, 60 and 57% for **9** at sodium nitrate concentrations, respectively, of 1, 2, 3 and 4 mol/L. With experimental values of 75, 61, 52 and 46%, the gradual precipitation both of the free ligands and the caesium complex at the surface of the membrane could be suggested. At $[NaNO_3]>1$ M, ligands settle on the surface of the membrane involving the decreasing of the permeate flux (generally from 46 L/h bar m^2 at 1 M to 1.5 L/h bar m^2 at 2 M). In fact, particle deposition is one of the fouling causes from these decreases in permeate flux.[49,50] With the use of ligands **12** and **15**, this phenomenon was amplified. Indeed, experimental values at 3 mol/L in sodium nitrate were of 39% although the theoretical retention rate should be close to 60% for both ligands.

Finally, when the concentration of sodium nitrate varied from 0.1 to 4 mol/L, no precipitation of **10** occurred, however the Cs^+ retention decreased rapidly until 16%, suggesting a weak Cs^+/Na^+ selectivity.

3. Conclusion:

The new synthesised host molecules **9**–**12** and **15** were obtained by different synthetic routes from both calix-(benzo)crown **6** and **7**. Their binding efficiencies for alkali-metal cations were determined by UV spectrophotometry in methanol and aqueous media. The results show that the efficiency of these hydrosoluble calix[4]benzocrowns-6 depends on the nature and number of grafted hydrophilic groups. Every ligand shows a more or less pronounced affinity for the studied alkali-metal cation, decreasing in all cases from the larger (Cs^+) to the smaller (K^+). Apart from the ligand **10**, the hydrosoluble receptors achieve a good compromise between preorganisation, steric hindrance and the cooperative effect of cation–arene and/or cation–phenolate interactions. Results concerning Cs^+/Na^+ separation by nanofiltration combined with these organic compounds fit well with UV–Vis analysis. Compounds **9**, **12** and **15** showed high Cs^+/Na^+ selectivity and allowed an efficient separation of traces of caesium separation by nanofiltration–complexation from a moderate salted medium ($[NaNO_3]=85$ g/L).

4. Experimental

4.1. Analytical instruments

^1H and ^{13}C NMR spectra were recorded on Brucker AC200 or AM300 (chemical shifts in ppm, J in Hz). Mass spectrometry was performed by electrospray technique, positive and negative mode. Elemental analysis was performed at Service Central d'Analyse, CNRS, Vernaison (France).

4.2. Synthesis

Solvents were commercial reagents and used without further purification. Dissolute compound **4**[45] was prepared according to reported procedures. Vicens procedure was used to prepare **5**, **6** and **7**. The synthesis of compounds **1** was described in a previous paper of water-soluble calixarenes-bis-crown-6.[34]

4.2.1. Ethyl 3,4-bis[2-(2-hydroxyethoxy)ethoxy]benzoate, 3. Ethyl 3,4-dihydroxybenzoate (20 g, 109 mmol) and potassium carbonate (63 g, 450 mmol) were stirred at room temperature in acetonitrile (540 mL) for 2 h. The mixture was then heated to reflux and 2-(2-chloroethoxy)ethanol (31.64 g, 254 mmol) was added. After 3 days, more potassium carbonate (24 g, 171 mmol) and 2-(2-chloro-ethoxy)ethanol (16.5 g, 132 mmol) were added and the mixture was kept to reflux 4 more days. The solvent was then evaporated and the residue dissolved in dichloro-methane, washed successively with 1N HCl, water, brine and dried over magnesium sulfate. Chromatography on silica column (60/40 CH_2Cl_2–acetone) afforded pure diol **3** as an oil (12 g, 30%). ^1H NMR spectrum ($CDCl_3$) δ (ppm) 1.37 (t, J=7.2 Hz, 3H, OCH_2CH_3); 3.55 (s, 2H, O*H*); 3.66–3.69 (m, 4H, OCH_2CH_2O); 3.74–3.77 (m, 4H, OCH_2CH_2O); 3.91–3.94 (m, 4H, OCH_2CH_2O); 4.18–4.21 (m, 4H, OCH_2CH_2O); 4.33 (q, J=6.6 Hz, 2H, OCH_2CH_3); 6.87 (d, J=8.8 Hz, Ar*H* on C-5); 7.57 (d, J=2.2 Hz, Ar*H* on C-2); 7.66 (dd, J=8.1, 2.2 Hz, Ar*H* on C-6). ES-MS (ES^+): 397.3 ($[M+K]^+$); 381.3 ($[M+Na]^+$).

4.2.2. Ethyl 3,4-bis[2-[2-[[(4-methylphenyl)sulfonyl]-oxy]ethoxy]ethoxy]benzoate, 5. To a solution of diol **3** (10.5 g, 29.30 mmol) and tosylchloride (27 g, 142 mmol) in dichloromethane (300 mL) at 0°C, triethylamine (14 g, 142 mmol) in dichloromethane (100 mL) was added drop-wise. After stirring at room temperature for 6 days, water (200 mL) was added. The organic layer was dried over magnesium sulfate, filtered, concentrated and purified by silica gel column chromatography (95/5 CH_2Cl_2–acetone) to give pure **5** (27 g, 86%) as an oil. ^1H NMR spectrum ($CDCl_3$) δ (ppm) 1.34 (t, J=7 Hz, 3H, OCH_2CH_3); 2.34 (s, 6H, CH_3); 3.70–3.77 (m, 8H, OCH_2CH_2O); 4.02–4.08 (m, 4H, OCH_2CH_2O); 4.11–4.15 (m, 4H, OCH_2CH_2O); 4.31 (q, J=7 Hz, OCH_2CH_3); 6.82 (d, J=8.8 Hz, ArH_{benzo}); 7.23 (d, J=8.1 Hz, 4H, ArH_{tosyl}); 7.48 (d, J=1.8 Hz, ArH_{benzo}); 7.62 (dd, J=8.5, 1.8 Hz, ArH_{benzo}); 7.72 (d, J=8.1 Hz, 4H, ArH_{tosyl}). ^{13}C NMR ($CDCl_3$) δ (ppm) 14.43, 21.59 (CH_3); 60.83 (OCH_2CH_3); 68.60, 68.87, 68.92, 68.97, 69.47, 69.59, 69.70, (OCH_2CH_2O), 112.7, 114.9 (Ar*C*H), 123.0, 144.9, 148.2, 152.8 (Ar*C*); 166.2 (*C*O). ES-MS (ES^+): 397.3 ($[M+K]^+$); 381.3 ($[M+Na]^+$).

4.2.3. Calix[4]arene-bis-[(4-methyl-1,2-phenylene)-crown-6], 6. A mixture of calix[4]arene (3.5 g, 8.24 mmol), potassium carbonate (11.4 g, 82.4 mmol) and ditosylate **4** (5.14 g, 8.24 mmol) in dry acetonitrile

(300 mL) was refluxed under Argon for 7 days. The same quantities of potassium carbonate and **4** in acetonitrile (50 mL) were added and reflux was continued for additional 10 days. After cooling to room temperature, the solvent was removed in vacuo. Dichloromethane (400 mL) was added and the suspension was neutralised by 1N HCl. The organic layer was washed with water, brine and dried over magnesium sulfate. The filtered solution was then concentrated and precipitated with methanol–diethylether to yield pure **6** as a white solid (5.18 g, 66%). ^{1}H NMR spectrum ($CDCl_3$) δ (ppm) 2.32 (s, 6H, CH_3); 3.47–3.72 (m, 24H, OCH_2CH_2O); 3.78 (s, 8H, ArCH_2Ar); 4.07–4.13 (m, 8H, OCH_2CH_2O); 6.69 (t, J=7.5 Hz, 4H, ArH_{calix}); 6.79 (d, J=7.6 Hz, 2H, ArH_{benzo}); 6.80 (s, 2H, ArH_{benzo}); 6.88 (d, J=7.6 Hz, 2H, ArH_{benzo}); 7.10 (d, J=7.5 Hz, 8H, ArH_{calix}). ^{13}C NMR spectrum ($CDCl_3$) δ (ppm) 21.03 (*C*H_3); 37.92 (Ar*C*H2Ar); 69.93, 70.11, 70.18, 70.31, 70.37 (O*C*H_2*C*H_2O); 116.1, 120.4, 122.6, 130.0 (Ar*C*H); 131.9, 134.1, 146.9, 149.2, 156.5 (Ar*C*). ES-MS (ES^+): 975.7 ($[M+Na]^+$). Anal. calcd for **6**·0.5H_2O ($C_{58}H_{65}O_{12.5}$): C, 72.41; H, 6.80; O, 20.78. Found: C, 72.23; H, 6.81; O, 20.21.

4.2.4. Calix[4]arene-bis-[(4-ethoxycarbonyl-1,2-phenylene)crown-6], 7. A mixture of calix[4]arene (3.5 g, 8.24 mmol), potassium carbonate (11.4 g, 82.4 mmol) and ditosylate **5** (5.64 g, 8.42 mmol) in dry acetonitrile (300 mL) was refluxed under Argon for 7 days. The same quantities of potassium carbonate and **5** in acetonitrile (50 mL) were added and reflux was maintained for additional 7 days. After cooling to room temperature, the solvent was removed under reduce pressure. Dichloromethane (200 mL) was added and the suspension was neutralised by 1N HCl. The organic layer was washed with water, brine and dried over magnesium sulfate. Pure **7** (3.6 g, 41%) was obtained as a white foam by purification on chromatography column (SiO_2, CH_2Cl_2–acetone 90/10). ^{1}H NMR spectrum ($CDCl_3$) δ (ppm) 1.40 (t, J=7.3 Hz, 6H, OCH_2CH_3); 3.57–3.62 (m, 16H, OCH_2CH_2O); 3.74–3.78 (m, 16H, ArCH_2Ar and OCH_2CH_2O); 4.18–4.20 (m, 8H, OCH_2CH_2O); 4.37 (q, J=7.3 Hz, 4H, OCH_2CH$_3$); 6.67 (t, J=7.3 Hz, 4H, ArH_{calix}); 6.97 (d, J=8.5 Hz, 2H, ArH_{benzo}); 7.07 (d, J=7.3 Hz, 8H, ArH_{calix}); 7.66 (d, J=2.2 Hz, 2H, ArH_{benzo}); 7.74 (d, J=8.5 Hz, 2H, ArH_{benzo}). ^{13}C NMR spectrum ($CDCl_3$) δ (ppm) 14.47 (*C*H_3); 37.78 (Ar*C*H_2Ar); 60.90 (O*C*H_2CH$_3$); 69.96, 69.99, 70.01, 70.07, 70.26, 70.44 (O*C*H_2*C*H_2O); 113.0, 115.6, 122.6, 124.3, 130.3 (Ar*C*H); 123.8, 134.1, 148.4, 153.0, 156.4 (Ar*C*); 166.4 (*C*O). ES-MS (ES^+): 1107.5 ($[M+K]^+$); 1091.4 ($[M+Na]^+$). Anal. calcd for **7**·0.25CH_2Cl_2 ($C_{62}H_{68}O_{16}$, 0.25 CH_2Cl_2): C, 68.56; H, 6.33; O, 23.47. Found: C, 68.64; H, 6.29; O, 23.29.

4.2.5. 5,11,17,23-Tetrabromocalix[4]arene-bis-[(4-bromo-5-methyl-1,2-phenylene)crown-6], 8. Compound **6** (2 g, 2.09 mmol) was stirred in dichloromethane (350 mL) at 0°C. Bromine (6.4 g, 40 mmol) in dichloromethane (20 mL) was added. After 5 h at room temperature, additional dichloromethane (200 mL) was added and the organic layer was washed with a solution of sodium metabisulfite 10%, water and brine, then dried over magnesium sulfate. Evaporation of solvent and purification by chromatography (SiO_2, CH_2Cl_2–MeOH 98/2) afforded pure **8** (2.18 g, 75%) as a white foam. ^{1}H NMR spectrum ($CDCl_3$) δ (ppm) 2.31 (s, 6H, CH_3); 3.39 (br t, 8H, OCH_2CH_2O); 3.51 (br t, 8H, OCH_2CH_2O); 3.74 (s, 8H, ArCH_2Ar); 3.81 (m, 8H, OCH_2CH_2O); 4.15 (m, 8H, OCH_2CH_2O); 6.81 (s, 2H, ArH_{benzo}); 7.08 (s, 2H, ArH_{benzo}); 7.21 (s, 8H, ArH_{calix}). ^{13}C NMR ($CDCl_3$) δ (ppm) 22.75 (*C*H_3); 37.52 (Ar*C*H_2Ar); 70.08, 70.10, 70.23, 70.26, 70.59, 70.70, 71.04, 71.10 (O*C*H_2*C*H_2O); 118.6, 120.1, 132.5 (Ar*C*H), 115.9, 131.3, 136.7, 148.7, 149.5, 151.3 (Ar*C*). ES-MS (ES^+): 1449.1 ($[M+Na]^+$). Anal. calcd for **8** ($C_{58}H_{58}O_{12}Br_6$): C, 48.85; H, 4.10; O, 13.46; Br, 33.62. Found: C, 48.76; H, 4.14; O, 13.85; Br, 33.50.

4.2.6. 5,11,17,23-Tetrahydroxycalix[4]arene-bis-[(4-hydroxy-5-methyl-1,2-phenylene)crown-6], 9. To a solution of **8** (0.5 g, 0.35 mmol) in dry tetrahydrofuran (100 mL) cooled at −78°C under argon was added *tert*-butyllithium (8.4 mL of a 1.7 M solution in pentane, 14.28 mmol). After 2 h, trimethyl borate (2.55 g, 24.47 mmol) was added and the solution was allowed to warm to room temperature. After 4 h under stirring, the reaction mixture was cooled again at −78°C and 3 M sodium hydroxide–hydrogen peroxide 35% (25 mL) was added dropwise. The mixture was again warmed to room temperature and stirred overnight. Sodium thiosulfate was carefully added to the solution and cooled to 0°C until saturation. After evaporation of tetrahydrofuran, water (50 mL) was added and the mixture was acidified with 2N HCl until 6<pH<7. The resulting precipitate was filtered off, rinsed with water and dissolved in methanol. Insoluble impurities were removed by filtration. Filtrate was evaporated to dryness and the residue dissolved in tetrahydrofuran. Precipitation with diethylether and filtration afforded pure **9** (0.228 g, 62%) as a white powder. ^{1}H NMR spectrum (DMSO-d_6) δ (ppm) 2.01 (s, CH_3); 3.16–4.00 (m, 32H, OCH_2CH_2O and 8H, ArCH_2Ar); 6.41 (br s, 2H, ArH_{benzo} and 8H, ArH_{calix}); 6.70 (s, 2H, ArH_{benzo}); 8.69 (br s, 6H, OH_{benzo} and OH_{calix}). ^{13}C NMR (DMSO-d_6) δ (ppm) 15.54 (*C*H_3); 37.48 (Ar*C*H_2Ar); 68.92, 69.50, 69.86, 70.15, 70.48 (O*C*H_2*C*H_2O); 103.8, 115.4, 120.39 (Ar*C*H), 116.0, 134.2, 141.5, 148.2, 149.1, 150.3, 151.8 (Ar*C*). ES-MS (ES^+): 1071.6 ($[M+Na]^+$). Anal. calcd for **9**·H_2O ($C_{58}H_{66}O_{19}$): C, 65.28; H, 6.23; O, 28.49. Found: C, 65.33; H, 6.15; O, 28.86.

4.2.7. 5,11,17,23-Tetracarboxycalix[4]arene-bis-[(4-carboxyl-5-methyl-1,2-phenylene)crown-6], 10. To a stirred solution of **8** (0.6 g, 0.42 mmol) dissolved in dry tetrahydrofuran (100 mL) at −78°C under argon was added *tert*-butyllithium in pentane (12.3 mL 1.7 M, 20.9 mmol). The resulting red solution was stirred at −78°C for 30 min and quenched with a large excess of CO_2 (g). HCl (10 mL, 6 M) was added to the reaction mixture and tetrahydrofuran was evaporated. The resulting precipitate was filtered, washed with water and dried under reduce pressure at 50°C overnight. Precipitation in acetone and filtration afforded pure **10** as a white powder (0.23 g, 45%). ^{1}H NMR spectrum (DMSO-d_6) δ (ppm) 2.49 (s, 6H, CH_3); 3.01 (br t, 8H, OCH_2CH_2O); 3.49–3.57 (m, 16H, OCH_2CH_2O); 3.62–4.01 (m, 8H, OCH_2CH_2O and 8H, ArCH_2Ar); 6.86 (s, 2H, ArH_{benzo}); 7.40 (s, 2H, ArH_{benzo}); 7.76 (s, 8H, ArH_{calix}); 12.54 (s, 6H, COO*H*). ^{13}C NMR (DMSO-d_6) δ (ppm) 21.18 (*C*H_3); 36.78 (Ar*C*H_2Ar); 68.01, 68.83, 69.29, 69.90, 70.00 (O*C*H_2*C*H_2O); 117.6, 119.5, 130.61 (Ar*C*H), 122.1, 124.8, 133.4, 135.1, 145.9, 152.5, 160.0 (Ar*C*); 167.1, 167.9

(*C*OOH). ES-MS (ES^+): 1241.1 ($[M+Na]^+$). Anal. calcd for **10**·$2H_2O$ ($C_{64}H_{62}O_{26}$): C, 61.64; H, 5.01; O, 33.35. Found: C, 61.95; H, 4.83; O, 33.46.

4.2.8. Calix[4]arene-bis-[(4-carboxyl-1,2-phenylene)-crown-6], 11. A mixture of **7** (0.4 g, 0.38 mmol) and potassium hydroxide (0.084 g, 1.52 mmol) in ethanol (15 mL) was stirred at reflux for 3 h. After cooling to room temperature, water (15 mL) was added followed by concentrated HCl (1.5 mL) and water (15 mL). The resulting white precipitate was filtered off, rinsed with water and dissolved in chloroform. The solution was dried over magnesium sulfate and evaporated to dryness to give pure **11** as a white powder (0.346 g, 90%). ^{1}H NMR spectrum (DMSO-d_6) δ (ppm) 3.32 (br s, 8H, OCH_2CH_2O); 3.43–3.48 (m, 8H, OCH_2CH_2O); 3.62–3.74 (m, 8H, ArCH_2Ar and 8H, OCH_2CH_2O); 4.1–4.2 (m, 8H, OCH_2-CH_2O); 6.57 (t, J=7.4 Hz, 4H, ArH_{calix}); 7.03 (d, J=7.4 Hz, 8H, ArH_{calix}); 7.13 (d, J=8.1 Hz, 2H, ArH_{benzo}); 7.52 (s, 2H, ArH_{benzo}); 7.63 (d, J=8.5 Hz, 2H, ArH_{benzo}); 12.71 (s, 2H, COO*H*). ^{13}C NMR spectrum (DMSO-d_6) δ (ppm) 36.81 (Ar*C*H_2Ar); 68.90, 69.12, 69.34, 69.52, 69.76 (O*C*H_2*C*H_2O); 113.2, 115.1, 121.9, 123.5, 129.7 (Ar*C*H); 133.7, 147.7, 152.5, 156.0, 156.1 (Ar*C*); 166.9(*C*O). ES-MS (ES^+): 1035.5 ($[M+Na]^+$). Anal. calcd for **11** ($C_{58}H_{60}O_{16}$): C, 68.83; H, 5.98; O, 25.29. Found: C, 68.34; H, 5.90; O, 24.98.

4.2.9. Calix[4]arene-bis-[[(4-(2-sulfooxy)ethylester)-1,2-phenylene]crown-6], dipotassium salt, 12. To a suspension of **11** (0.2 g, 0.197 mmol) and potassium carbonate (0.11 g, 0.788 mmol) in dry dichloromethane (50 mL) under argon was added 1,2,3-dioxathiolane-2,2-dioxide (0.1 g, 0.788 mmol). The mixture was heated at reflux for 48 h and then cooled to room temperature. The resulting precipitate was filtered off, washed with dichloromethane and triturated in dimethylsulfoxide. After filtration of insoluble salts, acetone was added to the filtrate and the resulting white precipitate was filtered off, washed with acetone and dried under vacuo to give pure **12** as a white powder (0.187 g, 71%). ^{1}H NMR spectrum (DMSO-d_6) δ (ppm) 3.52 (br t, 8H, OCH_2CH_2O); 3.63 (br t, 8H, OCH_2CH_2O); 3.70–3.74 (m, 8H, OCH_2CH_2O); 3.81 (s, 8H, ArCH_2Ar); 4.03 (t, J=5.2 Hz, 4H, OCH_2CH_2OSO$_3$K); 4.13–4.20 (m, 16H, OCH_2CH_2O); 4.39 (t, J=5.2 Hz, 4H, OCH_2CH_2OSO$_3$K); 6.56 (t, J=7.7 Hz, 2H, ArH_{calix}); 6.59 (t, J=7.7 Hz, 2H, ArH_{calix}); 7.11 (br d, 4H, ArH_{calix}); 7.13 (br d, 4H, ArH_{calix}); 7.18 (d, J=8.4 Hz, 2H, ArH_{benzo}); 7.65 (s, 2H, ArH_{benzo}); 7.70 (d, J=8.4 Hz, 2H, ArH_{benzo}). ^{13}C NMR spectrum (DMSO-d_6) δ (ppm) 36.39 (Ar*C*H_2Ar); 63.8, 63.84, 68.53, 68.71, 69.34, 69.60, 70.71, 70.76 (O*C*H_2*C*H_2O); 112.7, 114.2, 122.1, 122.4, 123.9, 130.1 (Ar*C*H); 134.1, 134.2, 147.6, 152.0, 156.1 (Ar*C*). ES-MS (ES^+): 1375.2 ($[M+K]^+$); 1359.2 ($[M+Na]^+$). Anal. calcd for **12**·H_2O ($C_{62}H_{68}O_{25}S_2K_2$): C, 54.95; H, 5.06; O, 29.52; S, 4.73. Found: C, 54.59; H, 5.10; O, 29.35; S, 5.18.

4.2.10. Calix[4]arene-bis-[(4-hydroxymethyl-1,2-phenylene)crown-6], 13. Under an atmosphere of argon, a solution of **7** (0.31 g, 0.289 mmol) in dry dimethoxyethane (20 mL) was added dropwise to a suspension of $LiAlH_4$ (0.46 g, 12.1 mmol) in dimethoxyethane (30 mL). The mixture was heated at reflux for 6 h. The excess of $LiAlH_4$ was destroyed by addition of water (0.5 mL), followed by addition of NaOH 15% (0.5 mL) and an additional quantity of water (1.5 mL). After 15 min under stirring, celite (5 g) was added and the mixture was stirred for 30 min. After filtration, the solvent was removed under reduced pressure and the residue chromatographed on silica gel (CH_2Cl_2–MeOH, 90/10) to give pure **13** (0.23 g, 80%) at a white foam. ^{1}H NMR spectrum (DMSO-d_6) δ (ppm) 3.28–3.35 (m, 8H, OCH_2-CH_2O and 2H, O*H*); 3.46–3.49 (m, 8H, OCH_2CH_2O); 4.1–4.2 (m, 8H, OCH_2CH_2O); 3.56–3.59 (m, 8H, OCH_2CH_2O); 3.73 (s, 8H, ArCH_2Ar); 4.01–4.03 (m, 8H, OCH_2CH_2O); 4.43 (s, 4H, CH_2OH); 6.58 (t, J=7.7 Hz, 4H, ArH_{calix}); 6.87 (d, J=8.2 Hz, 2H, ArH_{benzo}); 6.96 (d, J=8.2 Hz, 2H, ArH_{benzo}); 6.98 (s, 2H, ArH_{benzo}); 7.02 (d, J=7.4 Hz, 8H, ArH_{calix}). ^{13}C NMR spectrum (DMSO-d_6) δ (ppm) 36.92 (Ar*C*H_2Ar); 62.66 (Ar*C*H_2OH); 69.21, 69.42 (O*C*H_2*C*H_2O); 113.8, 115.2, 119.5, 121.9, 129.5 (Ar*C*H); 133.4, 136.1, 147.4, 148.6, 156.1 (Ar*C*). ES-MS (ES^+): 1023.7 ($[M+K]^+$); 1007.7 ($[M+Na]^+$). Anal. calcd for **13** ($C_{58}H_{64}O_{14}$): C, 70.72; H, 6.55; O, 22.73. Found: C, 70.34; H, 6.48; O, 23.19.

4.2.11. Calix[4]arene-bis-[(4-bromomethyl-1,2-phenylene)crown-6], 14. Phosphorus tribromide (150 μL, 1.62 mmol) was added to a stirred solution of **13** (0.53 g, 0.54 mmol) in dichloromethane (25 mL), cooled at 0°C. After 5 h of vigorous stirring, the reaction mixture was quenched with 50 mL of ice water. The organic layer was separated and the aqueous layer was further extracted with dichloromethane (50 mL). The combined extracts were washed with brine, dried over magnesium sulphate, and evaporated under reduced pressure. The residue was chromatographed on silica gel (CH_2Cl_2–MeOH, 95/5) to give pure **14** (0.54 g, 90%) as a white powder. ^{1}H NMR spectrum ($CDCl_3$) δ (ppm) 3.44–3.61 (m, 16H, OCH_2CH_2O); 3.66–3.73 (m, 8H, OCH_2CH_2O); 3.79 (s, 8H, ArCH_2Ar); 4.14–4.16 (m, 8H, OCH_2CH_2O); 4.52 (s, 4H, CH_2Br); 6.68 (t, J=7.4 Hz, 4H, ArH_{calix}); 6.91–7.09 (m, 6H, ArH_{benzo} and 8H, ArH_{calix}). ^{13}C NMR spectrum ($CDCl_3$) δ (ppm) 34.12 (*C*H_2Br); 37.86 (Ar*C*H_2Ar); 69.88, 69.97, 70.17, 70.25 (O*C*H_2*C*H_2O); 114.9, 116.3, 122.6, 122.7, 130.2 (Ar*C*H); 131.4, 134.1, 149.1, 149.4, 156.4 (Ar*C*). ES-MS (ES^+): 1050.3 ($[M+K]^+$); 1033.2 ($[M+Na]^+$). Anal. calcd for **14** ($C_{58}H_{62}O_{12}Br_2$): C, 68.91; H, 6.18; O, 18.99; Br, 15.81. Found: C, 68.96; H, 6.16; O, 19.24; Br, 15.84.

4.2.12. Calix[4]arene-bis-[[4-((*N*,*N*-diethanol)aminomethyl)-1,2-phenylene]crown-6], 15. Diethanolamine (0.382 g, 0.36 mmol) in dry dimethylsulfoxide (5 mL) was added to a stirred solution of **14** (0.2 g, 0.18 mmol) in dimethylsulfoxide (20 mL). The mixture was heated at 40°C under argon for 48 h. The solvent was evaporated under reduced pressure and the residue purified by chromatography on silica gel (CH_2Cl_2–MeOH–Et_3N 90/5/5) to give pure **15** (0.208 g, 50%). ^{1}H NMR spectrum ($CDCl_3$) δ (ppm) 2.68 (t, J=5.1 Hz, 8H, NCH_2CH_2OH); 3.43–3.45 (m, 8H, OCH_2CH_2O); 3.49–3.51 (m, 8H, OCH_2CH_2O); 3.55–3.59 (m, 8H, OCH_2CH_2O and 8H, NCH_2CH_2OH); 3.64 (s, 4H, ArCH_2N); 3.69 (s, 8H, ArCH_2Ar); 4.01–4.05 (m, 8H, OCH_2CH_2O); 5.28 (bs, 4H, O*H*); 6.60 (t, J=7.4 Hz, 4H, ArH_{calix}); 6.84 (s, 2H, ArH_{benzo}); 6.96–7.00 (m, 4H, ArH_{benzo} and 8H, ArH_{calix}). ^{13}C NMR spectrum ($CDCl_3$) δ (ppm) 37.82 (Ar*C*H_2Ar); 55.77, 58.96, 59.44 (N*C*H_2*C*H_2-OH and Ar*C*H_2N); 69.94, 70.10, 70.22 (O*C*H_2*C*H_2O);

115.2, 116.3, 122.4, 122.5, 130.1 (Ar*C*H); 132.2, 134.0, 148.3, 149.1, 156.4 (Ar*C*). ES-MS (ES^+): 1198.6 ($[M+K]^+$); 1181.1 ($[M+Na]^+$); 1159.8 ($[M+H]^+$). Anal. calcd for **15**·H_2O ($C_{66}H_{84}O_{17}N_2$): C, 67.32; H, 7.19; N, 2.38. Found: C, 67.88; H, 7.25; N, 2.52.

4.3. Stability constant measurement

UV–Vis studies were carried out in methanol and an aqueous medium containing 0.1 M NaOH at 25°C. Spectral changes of calixarenes solutions (2–3 mL) upon stepwise addition of alkali-metal salt into the measurement cell were recorded from 200 to 350 nm with a HP 8453 spectrophotometer using 1 cm path length quartz vessel. Chloride salts (KCl, RbCl, CsCl, Acros, p.a.) were preferred to nitrate salts to prevent NO_3^- overlapping of the ligand spectrum by the broad NO_3^- band.

4.4. Nanofiltration tests

Apparatus. A SEPA CF Membrane Cell (OSMONICS) was used with Nanomax 50 plane membrane (Millipore) which presents a surface area of 0.015 m^2, designed for tangential filtration. The retention (%) of a substance *i* was calculated as $R_i=100(1-C_{ip}/C_{ir})$ where C_{ip} is the concentration of *i* in the permeate and C_{ir} the concentration in the retentate. For all the NF results, sodium retention remained under 10% because the Nanomax membrane was chosen to be very permeable to monovalent ions. Tests were carried out using a transmembrane pressure of 0.06 MPa and a temperature of 293 or 333 K.

Chemicals and reagents. The metallic salts used for the NF tests were nitrates $NaNO_3$ (99%, Aldrich) and $CsNO_3$ (99.99%, Aldrich). Ligands were synthesised as described above.

Analytical. Caesium concentration was determined by atomic absorption spectroscopy (AAS) in an air–acetylene flame with a PU 9100X PHILIPS atomic absorption spectrometer. Each result is assumed to have a 5% standard deviation. Standards for AAS analysis were made of pure Cs^+ (caesium standards for ICP-AES analysis) and dissolved in the corresponding $NaNO_3$ and NaOH aqueous matrix.

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