Chloride ion recognition using thiourea/urea based receptors incorporated into 1,3-disubstituted calix[4]arenes†

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New calix[4]arene derivatives (**3–5**, **7–8**) of *cone* and 1,3-*alternate* conformations possessing thiourea/urea moieties have been synthesized and examined for their anion recognition abilities towards different anions like fluoride, chloride, bromide, iodide, nitrate and acetate by ^{1}H NMR and UV-Vis spectroscopy. Fitting the changes in the absorption spectra using nonlinear regression analysis indicates that all these compounds have strong binding affinity for chloride ions. The stoichiometry of the hydrogen bonded complexes is 1 : 1 (H : G) for receptor **3–5**, while it is 2 : 1 (H : G) with **7–8**. Chloride ion selective electrodes (ISEs) were also formed which showed excellent selectivity over all other anions tested.

Introduction

The selective recognition of anions plays an important role in biology, medicine, catalysis and environment.[1–2] Among anions, chloride is one of the most essential anions of biological relevance.[3] Biologically, chloride channels are essential for the maintenance of cell homeostasis. Mutation in the CFTR Cl^- channel leads to cystic fibrosis, one of the most prevalent in the case of Caucasian mammals.[4] Apart from this a plethora of genetic diseases have been associated with chloride channels.[5] The transport of chloride as HCl by prodigiosins through biological lipid bilayer membranes has been shown to uncouple lysosomal vacuolar type ATPases.[6] Thus, keeping in view these applications across these various diverse areas, the development of synthetic chloride receptors is an emerging topic in supramolecular chemistry.

Organic hosts with hydrogen bond donor groups have the potential to recognize anions with specific geometries.[7,8] The urea and thiourea moieties provide such effective and directional H-bonds for anion recognition. Calix[4]arene scaffolds incorporating one or more urea groups for anion binding offer diverse binding geometries.[9] Normally, in urea based receptors a major factor during anion–host interaction is competition from the solvation of anion and host initially present. Apart from this, in urea based systems, one has to take into account inter- and intramolecular hydrogen bonding. These bonds can be in direct competition with the detection of anions. However, such competing processes can provide discrimination against potential interferents, thus creating interesting selectivity patterns. These effects have also been studied for calixarenes.[10] While this work was in progress, Diamond *et al.* reported[11] a chloride selective optical sensor based on calix[4]arene again in 1,3-*alternate* conformation, having urea moieties.

Our research involves the design, synthesis and evaluation of calix[4]arene and thiacalix[4]arene based receptors selective for soft metal ions[12] and anions.[13] In a preliminary communication, we recently reported a chloride selective receptor **9** based on calix[4]arene of 1,3-*alternate* conformation.[14] Thus, in continuation of our research, we have now designed and synthesized five more chloride ion selective sensors based on calix[4]arenes in *cone* and 1,3-*alternate* conformations which have thiourea/urea moieties for interaction with anions. The presence of an electron withdrawing group ($-NO_2$) would be expected to increase the acidity of urea protons and hence enhance their anion binding ability through hydrogen bonding. The results show that compounds **3–5** and **7–8** have strong binding affinity for chloride ions as proved by solution state studies like UV and NMR. Chloride ion selective electrodes have also been formed with these receptors **3–5** and **7–8**, which show excellent selectivity over all other anions tested. There are some examples of calixarene based ionophores as ion selective electrodes (ISEs) for sensing of anions like carbonate,[9l] hydrogensulfite[15] and nitrate[16] ions, however, to the best of our knowledge the chloride ion selective electrodes based on calix[4]arenes bearing urea/thiourea moieties have not been reported so far.

Results and discussion

Synthesis

Calix[4]arene based thioureido/ureido receptors **3–5** (Scheme 1) and **7–8** (Scheme 2) were synthesized from known precursors **1**[17] and **6**,[13a] respectively. Condensation of calix-1,3-diamine **1**[17] with 2.0 mol equiv. of *p*-nitrophenylisothiocyanate/phenylisothiocyanate or *p*-nitrophenylisocyanate **2a–c** in dichloromethane gave thiourea **3**, **4** and urea **5** in 67%, 74% and 55% yields, respectively (Scheme 1).

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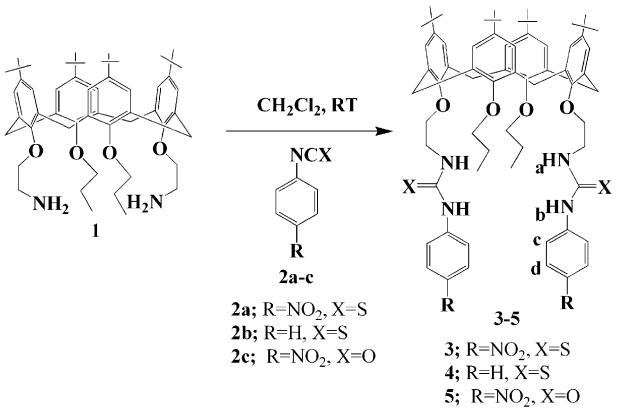
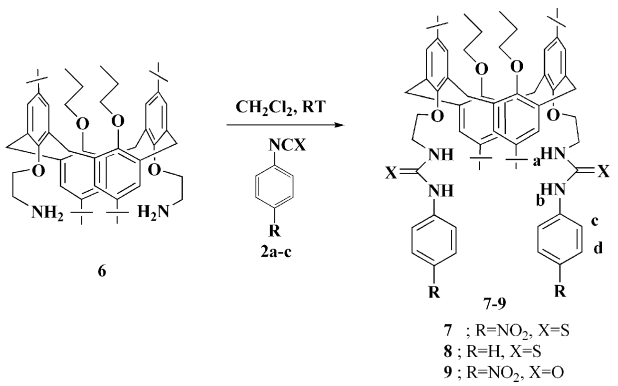
† Electronic supplementary information (ESI) available: ^{1}H and ^{13}C NMR data of compounds **3–5** and **7–8**, ^{1}H NMR studies, ISE studies. See DOI: 10.1039/b816275a/



Scheme 1 Synthesis of thiourea/urea derivatives **3–5**.



Scheme 2 Synthesis of thiourea/urea derivatives **7–9**.

Similarly, condensation of calix-1,3-diamine **6**[13a] of 1,3-*alternate* conformation with 2.0 mol equiv. of *p*-nitrophenylisothiocyanate/phenylisothiocyanate **2a–b** in dichloromethane gave thioureas **7** and **8** in 81% and 66% yields, respectively (Scheme 2). All the products (**3–5**, **7–8**) separated as pure solids after adding methanol/hexane to the dichloromethane solution, which gave a satisfactory elemental analysis after single crystallization.

The structures of all the compounds **3–5** and **7–8** were confirmed from their spectroscopic and analytical data. The IR spectra of **3**, **4**, **7** and **8** showed characteristic C=S stretching bands at 1568 cm^{-1}, 1545 cm^{-1}, 1582 cm^{-1} and 1532 cm^{-1}, respectively, whereas the ureido derivative **5** showed a C=O stretching band at 1651 cm^{-1}. The FAB mass spectra of all these compounds showed parent ion peaks corresponding to 1 : 2 condensation products. The ^{1}H NMR spectra of compounds **3–5** and **7–8** showed two singlets (18H each) corresponding to the *tert*-butyl protons, triplets (4H each) corresponding to the OCH_2 protons, two singlets (4H each) corresponding to aromatic protons, one singlet and a broad signal (2H each) for the amido protons. The bridging methylene protons of compounds **3–5** and **7–8** appear as AB quartets and as singlets, respectively. The ^{1}H NMR data suggest a C_{2v}-symmetric structure that is *cone* and 1,3-*alternate* conformations for compounds **3–5** and **7–8**, respectively. Compound **9**[14] was also prepared (Scheme 2) for making appropriate comparisons. All the receptors contain four urea/thiourea NH groups as H-bond donors for anions and two *p*-nitrophenyl groups for monitoring the anion-binding event in case of receptors **3**, **5** and **7**. The less acidic thiourea receptors **4** and **8** were analyzed for the anion sensing using ^{1}H NMR spectroscopy.

Anion binding studies

To evaluate the binding abilities of calix[4]arene receptors **3–5** and **7–8** towards different anions, we carried out UV-Vis and NMR experiments and prepared solid state ion selective electrodes. The anion recognition *via* hydrogen bonding interactions and deprotonation can be easily monitored by anion-complexation induced changes in UV-Vis and NMR spectra.

UV-Vis studies

Receptor **3** shows a UV-Vis absorption band at 339 nm in the absence of anions. On adding increasing amounts of tetrabutylammonium fluoride/acetate to the solution of receptor **3** in THF, the absorption peak at 339 nm decreases while a new peak gradually moving to longer wavelength finally reaching a maximum value at 470 and 451 nm appears (red shift of 131 and 112 nm, respectively) (Fig. 1A–B) and the color of the solution changes from colorless to orange-red. Similar results were obtained upon addition of Bu_4NOH to receptor **3**. Thus, we propose that the spectral changes in the case of **3** on the addition of fluoride/acetate ions are due to the removal of the thiourea proton (N–H_b); this suggests that a negatively charged *p*-nitroanilide ion was formed, which caused a significant increase in the charge density on thioureido nitrogen atom. This enhanced the charge-transfer interactions between electron-rich and electron-deficient moieties resulting in a visible color change.[18] There are a number of reports on mechanistic and spectroscopic explanations for deprotonation based anion sensing phenomenon of neutral hydrogen bond donor anion systems with anions like fluoride and acetate ions reported by Fabrrizzi *et al.*,[19] Gunnalaugsson *et al.*,[20] Gale *et al.*[21] and recently by Yatsimirsky *et al.*[22] for ureido derivatives.

Upon addition of increasing amounts of tetrabutylammonium chloride to a solution of receptor **3**, the absorption peak at 339 nm shifts to 357 nm (Fig. 1C). Similar shifts in the absorption peak were found in the cases of bromide, iodide and nitrate, where the absorption peak of receptor **3** shifts from 339 nm to 350, 346 and 346 nm, respectively.

Similarly, upon addition of increasing amounts of tetrabutylammonium chloride, bromide, iodide and nitrate, to a solution of receptor **7** (5×10^{-5} M) in THF, the absorption peak at 343 nm shifts to 357, 351, 349 and 344 nm, respectively (Fig. 2).

In the case of urea derivative **5** (5×10^{-5} M), an absorption band in the UV spectrum appeared at 333 nm in the absence of anions. Upon adding fluoride ion (Fig. 3A), the absorption peak at 333 nm decreases while a new peak gradually moving to longer wavelength with a red shift appeared at 369 nm with a clear isosbestic point at 335 nm. Upon addition of increasing amounts of chloride ion to the solution of receptor **5**, the absorption peak at 333 nm decreases while a new peak gradually moving to longer wavelength finally reaching

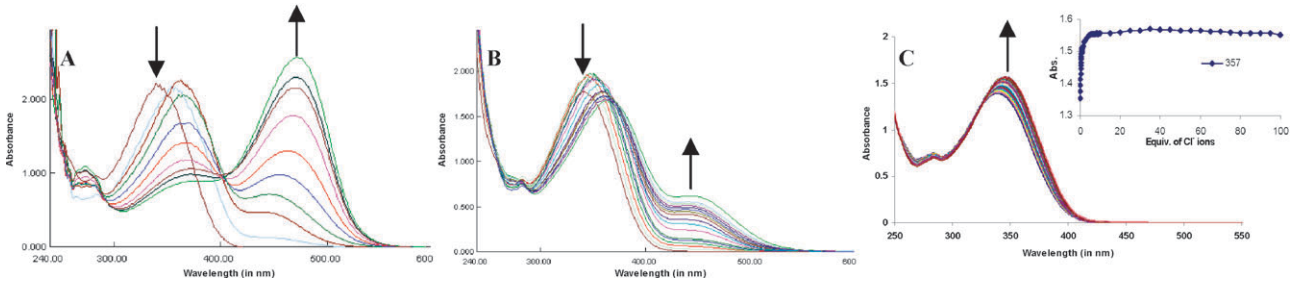


Fig. 1 UV-Vis absorption spectra of compound **3** (5×10^{-5} M) upon addition of (A) tetrabutylammonium fluoride (0–10 equiv.), (B) tetrabutylammonium acetate (0–4 equiv.) and (C) tetrabutylammonium chloride (0–20 equiv.) in THF. Inset showing the binding isotherm at selected wavelength in THF.

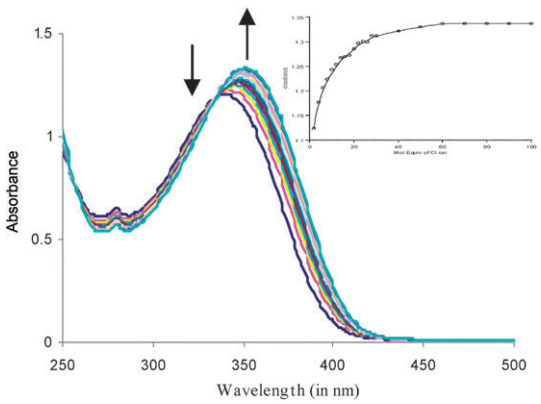


Fig. 2 UV-Vis absorption spectra of compound **7** (5×10^{-5} M) upon addition of tetrabutylammonium chloride (0–100 equiv.). Inset showing the binding isotherms at 357 nm in THF.

maximum value at 342 nm appeared (Fig. 3B). In the presence of anions like bromide, iodide and nitrate ion, there is a very small change in the absorption spectra of the receptor **5** from 333 nm to 340, 335 and 335 nm, respectively. This behavior is similar to the behavior of receptor **9** reported earlier by us.[14]

Fitting the changes in UV-Vis spectra of compounds **3**, **5** and **7** with various anions, using the nonlinear regression analysis program SPECFIT[23] (Table 1), the stability constant data show selective chloride ion recognition by these receptors, except in the case of receptor **5** where acetate has slightly better binding than chloride. Thus, from the above UV-Vis studies, it is clear that receptor **3** undergoes deprotonation of the acidic thiourea N–H in the presence of fluoride and acetate ions, whereas receptor **7** as already reported[13a] undergoes a hydrogen bonding interaction with these anions. Other anions like chloride, bromide, iodide and nitrate interact with these receptors (**3** and **7**) by hydrogen bonding. The urea based receptors **5** and **9** show hydrogen bonding interactions with all anions like fluoride, chloride, bromide, iodide, nitrate and acetate. Thus, from these results it may be concluded that the thiourea receptors **3** and **7** are more acidic than the urea receptors **5** and **9** as has been previously reported by Fabrrizzi *et al.*[24] Among the thiourea based receptors **3** and **7** of *cone* and 1,3-*alternate* conformation, respectively, the receptor **3** (*cone* conformer) is more acidic than the receptor **7** (1,3-*alternate* conformer) as receptor **3** undergoes deprotonation in presence of less basic anions like acetate while **7** does not undergo deprotonation.[13a]

^{1}H NMR studies

To evaluate the intermolecular interactions between the ureido calix[4]arene derivatives **3–5** and **7–9** with all anions like fluoride, chloride, bromide, iodide, acetate and nitrate, we carried out ^{1}H NMR studies in $CDCl_3$. Addition of different anions as their tetrabutylammonium salts to the solution of receptors in $CDCl_3$ results in the complexation induced shift of different protons of compounds **3–5** (ESI Table S11†) and compounds **7–9** (ESI Table S12†).

In general, addition of tetrabutylammonium fluoride to the solutions of compounds **3–5** and **7–9** in $CDCl_3$ results in the disappearance of ureido protons NH_a and NH_b, which indicates that either deprotonation of NH groups is taking place or the kinetics of anion exchange is on the NMR

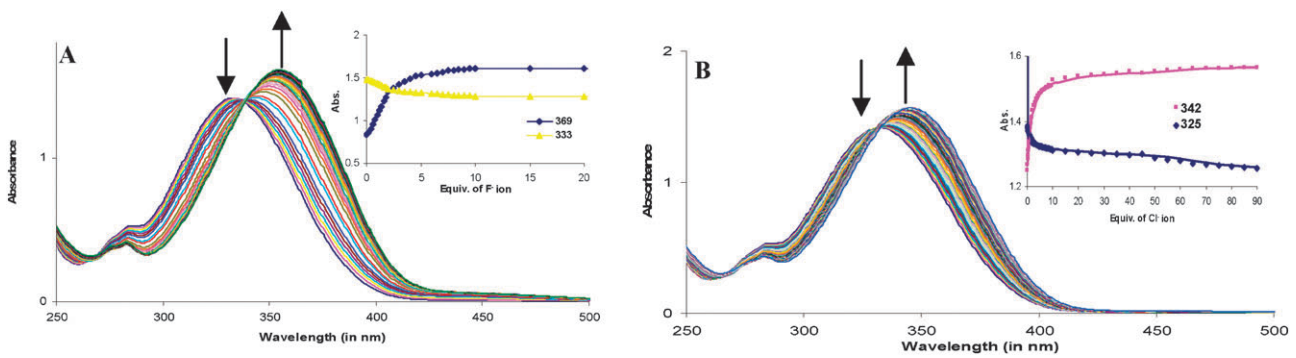


Fig. 3 UV-Vis absorption spectra of compound **5** (5×10^{-5} M) in THF upon addition of (A) tetrabutylammonium fluoride (0–100 equiv.) (B) tetrabutylammonium chloride (0–100 equiv.). Inset showing the binding isotherm at selected wavelengths in THF.

Table 1 Binding constants (Log β) of receptors **3–5** and **7–9** with various anions in THF at 298 K as calculated from SPECFIT programme (global analysis system V3.0 for 32-bit Window System)/WinEQNMR

Entry	Anion	**3**[a]	**4**[b]	**5**[a]	**7**[a]	**8**[b]	**9**[a14]
1	F^-	—	—	Log β_{11} 4.33 ± 0.09	—	—	Log β_{11} 4.01 ± 0.09
2	Cl^-	Log β_{11} 5.62 ± 0.02	Log β_{11} 3.68 ± 0.05	Log β_{11} 4.52 ± 0.09	Log β_{21} 7.41 ± 0.02	Log β_{21} 3.24 ± 0.23	Log β_{21} 6.54 ± 0.16
3	Br^-	Log β_{11} 4.87 ± 0.12	Log β_{11} 2.11 ± 0.19	Log β_{11} 4.08 ± 0.20	Log β_{11} 3.68 ± 0.10	Log β_{11} 1.19 ± 0.12	Log β_{11} 3.02 ± 0.02
4	I^-	Log β_{11} 3.67 ± 0.09	Log β_{11} 2.13 ± 0.12	Log β_{11} 3.25 ± 0.16	Log β_{11} 3.98 ± 0.16	Log β_{11} 2.52 ± 0.15	Log β_{11} 3.31 ± 0.16
5	NO_3^-	Log β_{11} 3.67 ± 0.32	Log β_{11} 1.91 ± 0.04	Log β_{11} 3.56 ± 0.24	Log β_{11} 3.22 ± 0.15	Log β_{11} 2.11 ± 0.31	Log β_{11} 3.12 ± 0.05
6	OAc^-	—	—	Log β_{11} 4.96 ± 0.05	Log β_{11} 6.01 ± 0.25		Log β_{11} 3.12 ± 0.05
	—				Log β_{12} 10.95 ± 0.30		

[a] Calculated using UV. [b] Calculated using WinEQNMR with NMR data.

timescale. Similar behavior was observed on addition of tetrabutylammonium acetate to solutions of compounds **3** and **9**. In the case of receptors **4**, **5**, **7** and **8** these ureido protons (NH_a and NH_b) undergo a downfield shift from 1.01–2.56 ppm and 0.90–2.76 ppm, respectively indicating hydrogen bonding phenomena taking place in these cases. Addition of 1.0 mol equiv. of tetrabutylammonium chloride to a solution of compounds **3–5** and **7–9** in $CDCl_3$ results in the complexation induced shift of the ureido protons NH_a and NH_b from 0.36–0.87 and 0.70–2.29 ppm, respectively, for receptors **3–5** (ESI Table S11†) and 0.38–1.47 and 0.61–.1.81 ppm, respectively, for receptors **7–9** (ESI Table S12†). In addition the H_c protons of the nitrophenyl moiety undergo a downfield shift of 0.51 and 0.54 ppm, in the case of receptors **3** and **7**, respectively, while in the presence of anions like bromide, iodide and nitrate the NH_a and NH_b protons undergo a downfield shift from 0.10–0.71 and 0.12–2.04 ppm for receptors **3–5**, respectively, and from 0.12–1.11 and 0.16–1.50 ppm, respectively, for receptors **7–9**. The greater downfield proton shifts in the case of chloride ions indicate strong hydrogen bonding between these receptors and chloride ions.

The stoichiometries of the complexes formed between receptors **3–5**, **7–9** and different anions were determined by Job's plot. Receptors **3–5** show a 1 : 1 (receptor–anion) complex formation with all the anions like chloride, bromide, iodide and nitrate ions (Fig. 4). However, in the case of

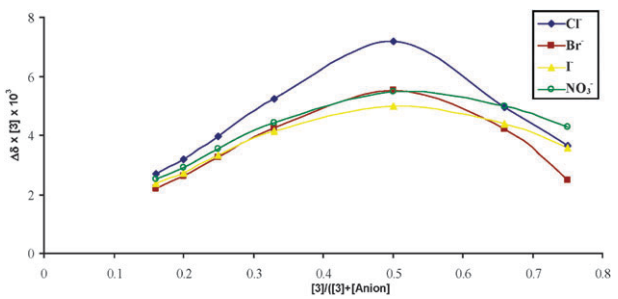


Fig. 4 Job's plot of compound **3** with tetrabutylammonium chloride, bromide, iodide and nitrate.

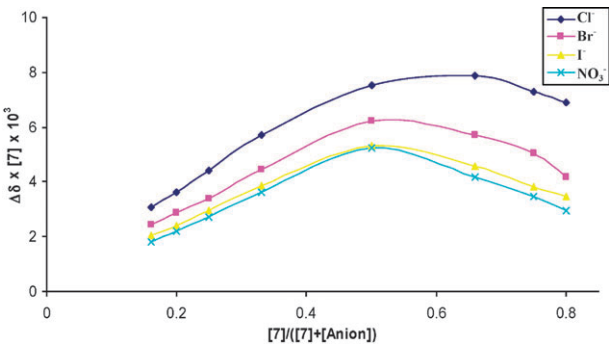


Fig. 5 Job's plot of compound **7** with tetrabutylammonium chloride, bromide, iodide and nitrate.

receptors **7–9**, the Job's plot shows a 2 : 1 (receptor–anion) complex formation with chloride ion, whereas with all other anions, these receptors show a 1 : 1 (receptor–anion) binding (Fig. 5).

Fitting the complexation induced shift of the thioureido protons of compound **4** with chloride, bromide, iodide and nitrate ions, using the EQNMR module,[25] gave binding constants log β_{11} = 3.68, 2.11, 2.13, 1.91, respectively. Similarly, in the case of receptor **8**, the binding constants were calculated to be log β_{21} = 3.24, β_{11} = 1.93, 2.52 and 2.11, respectively, with chloride, bromide, iodide and nitrate ions.

Thus from the above NMR results, it is clear that the ureido derivatives **3–5** of *cone* conformation form 1 : 1 (H : G) complexes with all the anions tested like chloride, bromide, iodide and nitrate. The ureido derivatives **7–9** of 1,3-*alternate* conformation form 1 : 1 complexes with anions like bromide, iodide and nitrate, but form a 2 : 1 (H : G) complex with chloride ion. It seems that there occurs a chloride ion induced dimerization of the receptors **7–9** of 1,3-*alternate* conformation.

A plausible explanation for dimerization of ureido calix[4]arene derivatives in our case might be due to the presence of an anion templating effect and the dimer reinforcement *via* additional complementary hydrogen bonds of individual calix[4]arenes.

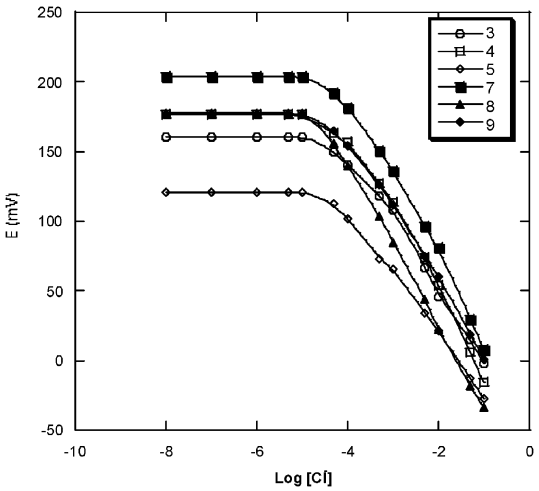


Fig. 6 Potential response curve of the membrane electrodes based on receptors **3–5** and **7–9** for chloride ion.

ISE studies

Based on the results of these binding studies (UV-Vis and NMR), we envisaged that it should be possible to construct chloride ion selective PVC membranes based on these calix podands. Thus, sensor membranes for all the receptors **3–5** and **7–9** were prepared and assembled as previously reported from our laboratory for silver ions.[12a]

The membrane electrodes **3–5** and **7–9** demonstrate a linear response for Cl^- ion in the concentration range from 1.0×10^{-5} to 1.0×10^{-1} mol dm^{-3} (Fig. 6). The limit of detection is 2.51×10^{-5} mol dm^{-3} as observed in the case of the electrodes based on receptors **3–5** and **7** and **9** and 1.50×10^{-5} mol dm^{-3} in the case of receptor **8**. The most important feature of an ion selective electrode is its response to its primary ion in the presence of various monovalent, divalent and trivalent anions. This is measured in terms of potentiometric selectivity coefficient ($K^{pot}_{A,B}$). Potentiometric selectivity coefficients (log $K^{pot}_{A,B}$) provide information about the preference of an ion selective electrode for secondary ion (B) relative to the primary ion (chloride ion). Potentiometric selectivity coefficients (log $K^{pot}_{A,B}$) were determined using the fixed interference method (FIM)[26] at a 1.0×10^{-2} M concentration of various interfering ions.

Table 2 shows the potentiometric selectivity coefficients data of the thiourea/urea derivatized *p-tert*-butylcalix[4]arene based PVC membrane electrodes for interfering anions relative to chloride ions. The selectivity coefficient pattern clearly indicates that the electrodes are selective to chloride over a number of other anions. The selectivity coefficient values obtained for different secondary anions with the proposed chloride ion selective electrodes suggest that these anions do not interfere in the normal working of the proposed electrodes even when present at the high concentration level of 1.0×10^{-2} M.

Conclusion

To sum up, we have reported here the first example of chloride ion selective electrodes based on calix[4]arenes of *cone* and 1,3-*alternate* conformation possessing urea and thiourea. The solution state studies show that the chloride ion is more strongly bound by the thiourea based receptors **3** and **7**, than by the urea based receptor **5** due to the increased acidity of the thiourea receptors over their urea counterparts.

Experimental

All reagents were purchased from Aldrich and were used without further purification. THF was dried over sodium and benzophenone and kept over molecular sieves overnight before use. UV Spectra were recorded on SHIMADZU UV-1700 spectrophotometer, with a quartz cuvette (path length: 1 cm). The cell holder was thermostated at 25 °C. ^{1}H and ^{13}C NMR spectra were recorded on JEOL-FT NMR-AL 300 MHz spectrophotometer using $CDCl_3$/DMSO-d_6 as solvent and TMS as internal standards. UV studies were performed in THF AR grade. All spectrophotometric titrations curve were fitted with SPECFIT\32 software. Experimental procedure for UV-Vis and ^{1}H NMR titrations and methods for preparation of membranes is given in the ESI.†

Syntheses

General procedure for the synthesis of receptors 3–5 and 7–8. 2.2 Equiv. of *p*-nitrophenyl isothiocyanate (**2a**)/phenyl isothiocyanate (**2b**)/*p*-nitrophenyl isocyanate (**2c**) were added to a solution of 5,11,17,23-tetra-*tert*-butyl-25,27-bis(2-aminoethoxy)-26,28-dipropoxycalix[4]arene **1/6** (81.8 mg, 0.10 mmol, 1.0 equiv.) in dry CH_2Cl_2 (20 mL). The resulting mixture was stirred at room temperature. After the completion of the reaction (TLC, 6 h) the solvent was removed under vacuum. The residue in the case of receptors **3–5** was then recrystallized from dichloromethane and methanol to give the desired compound while in the case of receptors **7–8** it was recrystallized from dichloromethane and hexane.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,27-bis(*p*-nitrophenyl-thioureido ethoxy)-26,28-dipropoxy-calix[4]arene 3. Yield (0.079 g, 67%). mp 196 °C. IR ν_{max} (KBr, cm^{-1}) 3220 (NH), 1568 (C=S), 1304. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.27 (s, 2H, NH), 8.12 (d, J = 9.0 Hz, 4H, H_d), 7.83 (br, 2H, NH), 7.59 (d, J = 9.0 Hz, 4H, H_c), 7.17 (s, 4H, ArH), 6.45 (s, 4H,

Table 2 Selectivity coefficient values of chloride ion selective electrode **3–5** and **7–9**

Receptor	Secondary ion	NO_2^-	Tartrate	Citrate	CO_3^{2-}	HCO_3^-	OAc^-	NO_3^-	NCS^-	SO_4^{2-}	OH^-	F^-	N_3^-	ClO_4^-	Br^-	I^-
3	Log $K^{pot}_{A,B}$	−2.80	−3.80	−3.93	−3.65	−2.70	−3.00	−3.00	−1.20	−3.62	−2.20	−3.00	−2.10	−2.45	−0.50	−1.00
4	Log $K^{pot}_{A,B}$	−3.10	−3.60	−4.08	−3.60	−2.75	−3.20	−3.20	−1.00	−4.20	−2.10	−3.00	−2.20	−2.20	−1.90	−1.20
5	Log $K^{pot}_{A,B}$	−3.00	−3.80	−4.03	−3.70	−2.65	−3.10	−3.05	−0.50	−4.05	−2.70	−3.00	−2.55	−2.70	−1.00	−1.00
7	Log $K^{pot}_{A,B}$	−3.00	−3.95	−4.23	−3.70	−3.00	−3.00	−2.70	−0.20	−4.10	−2.20	−2.70	−2.20	−2.75	−0.95	−1.10
8	Log $K^{pot}_{A,B}$	−3.30	−4.50	−4.31	−4.05	−2.70	−3.05	−3.05	−1.45	−4.60	−2.55	−2.80	−2.60	−3.10	−1.35	−1.15
9[14]	Log $K^{pot}_{A,B}$	−3.00	−3.75	−4.31	−3.65	−2.70	−3.00	−2.60	−1.40	−4.00	−2.10	−2.65	−2.50	−2.70	−1.30	−1.80

ArH), 4.29 (d, J = 12.9 Hz, 4H, $ArCH_2Ar$), 4.23 (m, 8H, OCH_2, NCH_2), 3.80 (t, J = 5.1 Hz, 4H, OCH_2), 3.26 (d, J = 12.9 Hz, 4H, $ArCH_2Ar$), 1.68–1.76 (m, 4H, CH_2), 1.36 (s, 18H, $C(CH_3)_3$), 0.82 (s, 18H, $C(CH_3)_3$), 0.81 (t, J = 7.5 Hz, 6H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 180.7, 153.4, 151.3, 146.2, 144.9, 143.9, 135.1, 131.4, 126.2, 124.9, 124.7, 122.2, 78.1, 71.9, 45.5, 34.2, 33.7, 31.7, 31.3, 31.1, 22.8, 10.1. FAB-MS m/z 1179 $(M + 1)^+$. Anal. calcd for $C_{68}H_{86}N_6O_8S_2.H_2O$: C, 68.23; H, 7.36; N, 7.02; S, 5.35%. Found: C, 68.19; H, 7.64; N, 6.91; S, 4.95%.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,27-bis(phenylthioureido ethoxy)-26,28-dipropoxy-calix[4]arene 4. Yield (0.080 g, 74%). mp 227 °C. IR ν_{max} (KBr, cm^{-1}) 3220 (NH), 1545 (C═S). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 7.74 (s, 2H, N–H), 7.38 (t, J = 7.2 Hz, 4H, ArH), 7.21–7.28 (m, 6H, ArH), 7.03 (s, 8H, ArH), 6.82 (br s, 2H, NH), 6.45 (s, 4H, ArH), 4.24–4.28 (m, 12H, $ArCH_2Ar$, OCH_2, NCH_2), 3.71 (t, J = 7.5 Hz, 4H, OCH_2), 3.10 (d, J = 12.6 Hz, 4H, $ArCH_2Ar$), 1.74–1.82 (m, 4H, CH_2), 1.29 (s, 18H, ^{t}Bu), 0.86 (t, J = 7.5 Hz, 6H, CH_3), 0.84 (s, 18H, ^{t}Bu). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 181.2, 153.7, 152.1, 145.3, 144.3, 136.8, 134.8, 131.8, 129.8, 126.7, 125.7, 125.0, 124.6, 107.2, 77.7, 72.1, 45.8, 34.0, 33.6, 31.6, 31.2, 31.1, 23.1, 10.3. FAB-MS m/z 1089 $(M + 1)^+$. Anal. calcd for $C_{68}H_{88}N_4O_4S_2$: C, 74.96; H, 8.14; N, 5.14; S, 5.89%. Found: C, 73.19; H, 8.01; N, 4.52; S, 4.95%.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,27-bis(*p*-nitrophenylureidoethoxy)-26,28-dipropoxy-calix[4]arene 5. Yield (0.063 g, 55%). mp 177 °C. IR ν_{max} (KBr, cm^{-1}) 3335 (NH), 1651 (C═O). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.12 (d, J = 9.0 Hz, 4H, H_d) 8.10 (br, 2H, NH), 7.59 (d, J = 9.0 Hz, 4H, H_c), 7.15 (s, 4H, ArH), 6.68 (br, 2H, NH), 6.44 (s, 4H, ArH), 4.32 (d, J = 12.6 Hz, 4H, $ArCH_2Ar$), 4.19 (t, J = 5.1 Hz, 4H, OCH_2), 3.85 (br, 4H, NCH_2), 3.77 (t, J = 7.5 Hz, 4H, OCH_2), 3.18 (d, J = 12.6 Hz, 4H, $ArCH_2Ar$), 1.71–1.76 (m, 4H, CH_2), 1.35 (s, 18H, $C(CH_3)_3$), 0.81 (s, 18H, $C(CH_3)_3$), 0.81 (t, J=7.5 Hz, 6H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 155.6, 153.4, 151.5, 145.8, 144.5, 142.0, 135.4, 131.5, 125.9, 125.2, 124.6, 117.9, 77.8, 73.0, 40.7, 34.1, 33.6, 31.7, 31.1, 31.0, 22.9, 10.2. FAB-MS m/z 1147 $(M + 1)^+$. Anal. calcd for $C_{68}H_{86}N_6O_{10}$: C, 71.20; H, 7.50; N, 7.34%. Found: C, 71.15; H, 7.79; N, 6.97%.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,27-bis(*p*-nitrophenylthioureido ethoxy)-26,28-dipropoxy-calix[4]arene 7. Yield (0.065 g, 85%). mp 207 °C. IR ν_{max}(KBr, cm^{-1}) 3220(NH), 1582 (C═S), 1304. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.23(s, 2H, NH), 8.18(d, J = Hz, 4H, H_d), 7.56(d, 4H, H_c), 7.07(s, 4H, ArH), 7.03 (s, 4H, ArH), 6.86 (br, 2H, NH), 3.83 (s, 8H, $ArCH_2Ar$), 3.67(t, J = 5.1 Hz, 4H, NCH_2), 3.62(t, J = 8.1 Hz, 4H, OCH_2), 3.36(t, J = 5.1 Hz, 4H, OCH_2), 1.27(s, 18H, $C(CH_3)_3$), 1.19(s, 18H, $C(CH_3)_3$), 1.11–1.90(m, 4H, CH_2), 0.73(s, 6H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 180.3. 155.2, 152.5, 144.7, 134.2, 132.7, 127.0, 126.3, 125.1, 122.0, 72.3, 45.6, 39.1, 34.1, 33.9, 31.5, 31.4, 22.0. 9.7. FAB-MS m/z 1179 $(M + 1)^+$. Anal. calcd for $C_{68}H_{86}N_6O_8S_2.H_2O$: C, 68.22; H, 7.35; N, 7.02; S, 5.35%. Found: C, 68.47; H, 7.73; N, 6.91; S, 4.95%.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,27-bis(phenylthioureidoethoxy)-26,28-dipropoxy-calix[4]arene 8. Yield (0.072 g, 66%). mp 214 °C. IR ν_{max}(KBr, cm^{-1}) 3300 (NH), 1532 (C═S). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 7.69 (s, 2H, N–H) 7.41 (t, J = 7.5 Hz, 4H, ArH), 7.26 (t, J = 7.5 Hz, 2H, ArH), 7.18 (d, J = 8.1 Hz, 4H, ArH), 6.98 (s, 8H, ArH), 6.25 (br, 2H, NH), 3.80 (s, 8H, $ArCH_2Ar$), 3.31 (t, J = 7.5 Hz, 4H, OCH_2), 3.17 (br t, 4H, NCH_2), 3.01 (br t, 4H, OCH_2), 1.26 (s, 18H, ^{t}Bu), 1.21 (s, 18H, ^{t}Bu), 0.99–1.07 (m, 4H, CH_2), 0.66 (t, J = 7.5 Hz, 6H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 180.6, 154.9, 153.6, 144.9, 144.0, 134.0, 133.1, 129.9, 126.6, 126.5, 126.2, 124.6, 72.2, 68.0, 45.3, 39.0, 34.0, 33.8, 31.6, 31.4, 21.8, 9.7. FAB-MS m/z 1089 $(M + 1)^+$. Anal. calcd for $C_{68}H_{88}N_4O_4S_2$ C, 74.96; H, 8.14; N, 5.14; S, 5.89%. Found: C, 74.01; H, 7.92; N, 4.92; S, 4.99%.

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