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Novel anion receptors based on thiacalix[4]arene derivatives

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Abstract—Starting from the thiacalix[4]arene tetraacetate, novel derivatives bearing four ureido or thioureido functions on the lower rim have been prepared. As proven by NMR titrations, these compounds can bind anions via hydrogen bonding interactions and represent the first example of anion receptors in the thiacalixarene series.

1. Introduction

Anion recognition, complexation and transport were recognised only rather recently as a very important part of supramolecular chemistry.[1] Despite many indispensable roles in the biochemical processes and pathways, where anions are frequently engaged in enzymatic reactions as substrates and/or cofactors, the supramolecular chemistry of anions is still quite unexplored if compared with that of cations.

There are several different strategies used for anion complexation so far.[2] Basically, the receptors can be divided into two main groups: (i) charged systems exploring electrostatic interactions with positively charged species (polyammonium[3] and guanidinium[4] salts, quaternary ammonium salts); (ii) neutral systems[5] using other kind of interactions, such as donor–acceptor interactions (receptors based on the Lewis acids), hydrogen bonds, hydrophobic effects etc. Significant progress has been made, especially in the design and synthesis of neutral receptors based on the hydrogen bonding interactions. Among them, systems employing amidic and (thio)urea moieties[6] have been proven especially efficient in the design of anion receptors.

Calix[*n*]arenes are very well-known building blocks[7] in supramolecular chemistry, frequently used as molecular scaffolds for the synthesis of more elaborated structures. There are many examples in the literature, where substituted calixarenes were used for anion complexation.[8] Many different systems exploiting the HB interactions,[9] Lewis acids,[10] or charged receptors[11] have been introduced for anion recognition. Another interesting group of anion receptors is represented by compounds capable of ion-pair recognition (ditopic receptors[12]), where the calixarene skeleton holds both cation- and anion-complexing functions.[13]

There is much evidence that ureido functions appended to calixarene can form a suitably pre-organized cavity (depending on the calixarene conformation used) with pronounced anion recognition capability. We[14] and others[15] have reported the *cone* and the *1,3-alternate* calixarenes bearing urea or thiourea functions on the upper/lower rim that can bind anions such as halogenides and carboxylates.

Thiacalixarenes[16] have appeared recently as novel members of the calixarene[7] family. The presence of sulfur atoms instead of CH_2 groups induces many novel features[17] compared with 'classical' calixarenes. Thiacalix[4]arenes exhibit a broad range of interesting functions such as different size and conformational behaviour, different complexation ability, easy oxidation of –S– bridges etc., which makes these compounds good candidates for many applications in supramolecular chemistry.

In this paper we report on the synthesis of thiacalix[4]arene derivatives bearing ureido or thioureido functions on the lower rim, which can serve as anion receptors. To the best of our knowledge, this is the first example of anion recognition in thiacalixarene series.

2. Results and discussion

2.1. Synthesis of receptors

The synthesis started from parent thiacalixarene **1**, which

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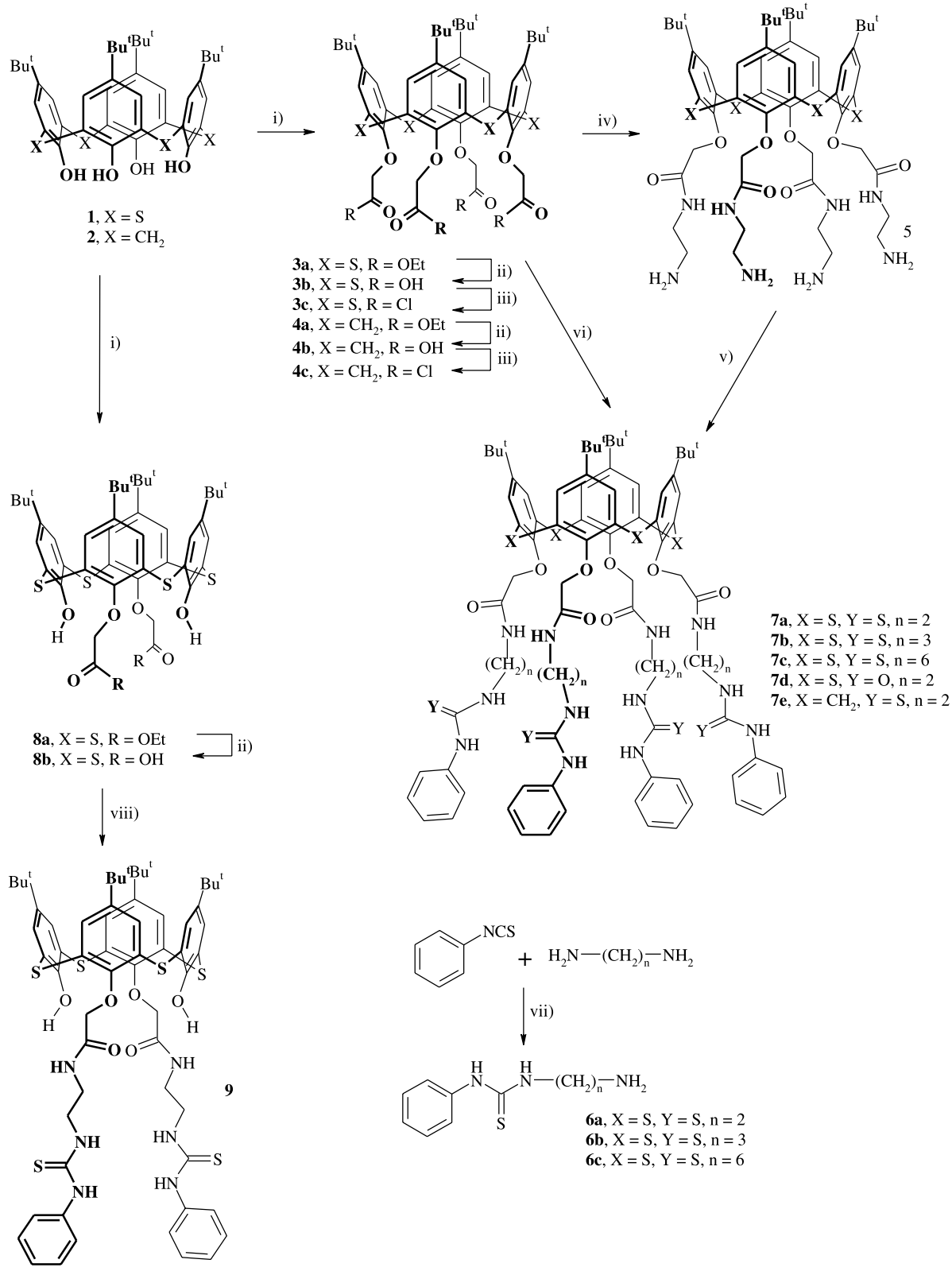
were transformed into the *cone* tetraacetate **3a** (75% yield) by alkylation with ethyl bromoacetate in refluxing acetone[18] using Na_2CO_3 as a base. Ester **3a** was hydrolysed (NaOH, aqueous ethanol, reflux) to yield the carboxylic acid **3b** in almost quantitative yield (Scheme 1). The carboxylic acid **3b** was then reacted with oxalyl chloride to yield the corresponding acyl chloride[19] **3c**. The crude chloride was used without purification for subsequent condensation



Scheme 1. (i) $BrCH_2COOEt/Na_2CO_3$, acetone, reflux (**3a**, 75%, **4a**, 55%, **8a**, 51%); (ii) NaOH, EtOH/water, reflux (**3b**, 99%, **4b**, 99%, **8b**, 99%); (iii) oxalyl chloride/CCl_4, reflux (**3c**, **4c**, quant.); (iv) ethylenediamine/THF, rt; (v) phenyl isocyanate/*i*-PrOH, reflux (8% from **3a**); (vi) **6a**–**6c**/Et_3N/THF, rt (**7a**, 23%; **7b**, 26%; **7c**, 22%; **7e**, 7%); (vii) *i*-PrOH, rt (**6a**, 46%; **6b**, 30%; **6c**, 17%); (viii) **6a**/CDI/DMF, rt (**9**, 54%).

(THF/EtN_3, rt) with the amino component **6a–6c**. The corresponding tetraamides **7a–7c** immobilised in the *cone* conformation were obtained after purification by preparative TLC (silica gel) in 23, 26 and 22% yields, respectively.

The reaction of tetraacetate **3a** with an excess of 1,2-ethanediamine led to an intractable mixture of tetraamine **5**, partly substituted and bridged compounds, that was used without purification in the next step-reaction with phenyl isocyanate. This procedure gave the appropriate urea derivative **7d** in 8% yield (overall yield from **3a**). Interestingly, attempts at the direct aminolysis of tetraester **3a** with amines **6a–6b** were unsuccessful as only very complicated reaction mixtures were obtained.

To compare the complexation properties of novel thiacalix[4]arene derivatives with classical calixarene series, tetrathioureido receptor **7e** was prepared using essentially the same strategy as described for **7a–7c**. Another model compound, dithioureido receptor **9**, was synthesised in order to evaluate the role of preorganisation and multiplicity of ureido functions on the lower rim of thiacalixarene. The synthesis followed the above strategy with one exception-the amidic bond in **9** was constructed using the reaction of free dicarboxylic acid **8b** with amine **6a** after activation with *N*,*N*′-carbonyl diimidazole in 54% yield.

2.2. Structure assignments and the NMR complexation study

The structures of novel ureido/thioureido calixarenes were proven using the combination of ^{1}H NMR spectroscopy and mass spectroscopy (ESI-MS or FAB MS). The full assignment of ^{1}H and ^{13}C NMR spectra was done using gCOSY, gHSQC and gHMBC methods. As the synthetic pathway started from the conformationally immobilised *cone* tetraacetates **3a** and **4a** of known structures,[18a] the conformational assignment of products was not necessary. The conformational preferences of thiacalixarene diacetate **8a** are also known,[20] anyhow the structure of derivative **9** was proved independently by one-dimensional DPFGSE-NOE experiments. The ESI MS spectra of all receptors usually showed the two most intense signals corresponding to the molecular peak $[M+Na]^+$ and to the doubly charged species $[M+2Na]^{2+}$. Thus, derivative **7e** exhibits two peaks at $m/z=817.64$ $[M+2Na]^{2+}$ (65% int.) and 1611.4 $[M+Na]^+$ (100% int.), respectively.

As the ^{1}H NMR spectra are almost uninfluenced by the change of solvent polarity ($CDCl_3$, $CDCl_3$–$CD_3CN=4:1$, DMSO-d_6) we can conclude that the possible intra-/intermolecular hydrogen bonds are very week or absent under the measuring conditions.

The complexation abilities of receptors **7** and **9** towards Cl^- anion were studied by ^{1}H NMR titrations in $CDCl_3$–$CD_3CN=4:1$ (v/v) mixture. The addition of Bu_4NCl resulted in the complexation-induced shift of NH signals ($\Delta\approx200$ Hz). All titration experiments were performed with constant concentration of receptor (approx. 2×10^{-4} M) and an increasing concentration of anion added. These experiments led to well reproducible binding isotherms corresponding to 1:1 binding (Fig. 1) that were analysed using an original nonlinear curve-fitting program[21] and statistically treated for several various signals. To confirm the stoichiometry of anion complexation, Job plots were constructed from ^{1}H NMR titration data. In all cases studied, the formation of the 1:1 complexes was clearly substantiated (Fig. 2).

The highest complexation-induced NMR shifts within the receptor molecules are those of the NH signals. As shown in Figure 3, both ureido NH protons (Nr. 12 and 14) in **7a** are the most downfield shifted signals after the addition of 5 equiv of chloride. This clearly indicates that the ureido/thioureido groups create a binding site, which is responsible for anion binding via synchronous hydrogen bonding interactions. The comparison with classical calix[4]arene derivative **7e** shows that the binding modes are identical in both systems.

As shown in Table 1, the corresponding complexation constants depend on the length of the lower rim alkylene chains. The lower is the rigidity of the system (the longer

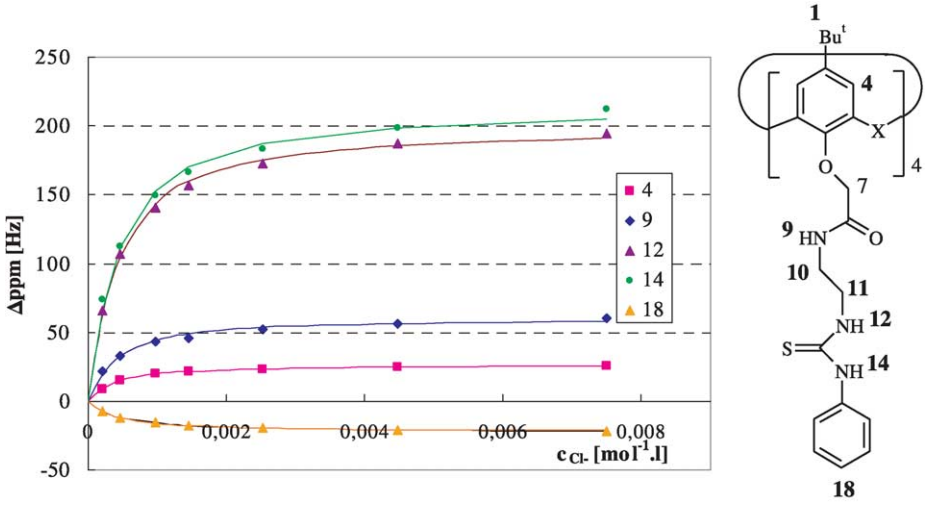


Figure 1. ^{1}H NMR titration curves of **7a** with $Bu_4^+NCl^-$ (300 MHz, $CDCl_3$–$CD_3CN=4:1$v/v, 298 K), several various ^{1}H signals used (see the numbering scheme).

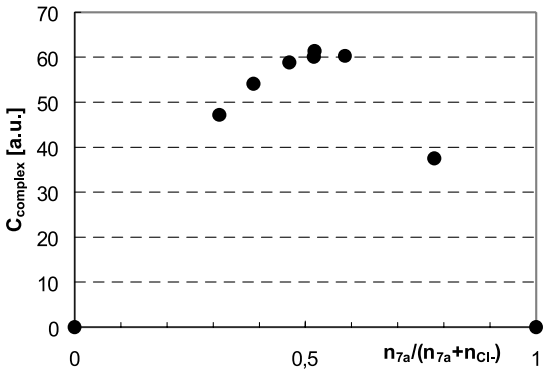


Figure 2. Job plot for the **7a**+$Bu_4N^+Cl^-$ system (^{1}H NMR, 300 MHz, $CDCl_3$–CD_3CN=4:1v/v).

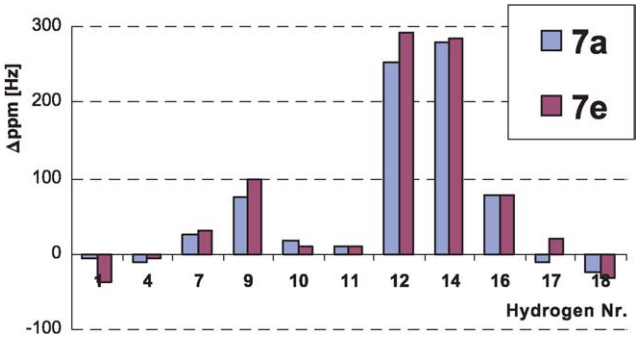


Figure 3. Complexation induced ^{1}H NMR chemical shifts in **7a** and **7e** after addition of 5 equiv of $Bu_4N^+Cl^-$ (300 MHz, $CDCl_3$–CD_3CN=4:1 v/v).

Derivatives **7** could, in principle, operate as ditopic receptors for ion-pair complexation. These molecules contain a second binding site at the thiacalix[4]arene lower rim formed by four amidic groups potentially capable of synchronous binding of alkaline metal cations. The complexation ability for sodium cations in $CDCl_3$ was determined by ^{1}H NMR titrations with Kobayashi reagent $NaB[3,5\text{-}(CF_3)_2C_6H_3]_4$ (sodium salt well soluble in apolar solvents). It was found that complexation constants of **7a** ($K_{Na}=1960\ M^{-1}$) and **7d** ($K_{Na}=520\ M^{-1}$) are very small if compared with classical calixarene derivative **7e** ($K_{Na}>10^5\ M^{-1}$).

To test the influence of cation complexation on the anion recognition the ^{1}H NMR titrations of preformed sodium complex was carried out. Unfortunately, as the NH signals are invisible or extensively broadened under the conditions used, they cannot be used for the construction of titration curves. The addition of Bu_4NCl to the mixture of **7a** and excess of Kobayashi reagent (5 equiv) led to only minor changes in chemical shifts of aromatic or CH_2 signals. As shown in Figure 4 the titration curves do not correspond to simple 1:1 binding. Rather than synchronous complexation of cation and anion they reflect more complex process. As the separately obtained complexation constants for Na^+ and Cl^- are of the same order ($K_{Na}=1960\ M^{-1}$ vs $K_{Cl}=3480\ M^{-1}$), it seems highly probable that both processes (cation vs anion complexations) are competitive rather than cooperative. The same phenomenon was found for thiacalixarene **7d** (Fig. 5).

In conclusion, easily accessible thiacalix[4]arene tetraacetate in the *cone* conformation was transformed into the

Table 1. Complexation constants K of receptors **7** and **9** towards selected anions (^{1}H NMR, $CDCl_3$–CD_3CN=4:1 v/v, 25 °C, 300 MHz)

Anion	K_C [mol^{-1} l]					
	7a	**7b**	**7c**	**7d**	**7e**	**9**
Cl^-	3480	1900	1790	4300	2670	220
Br^-	830	—	—	990	780	—
I^-	100	—	—	240	250	—
CN^-	1740	—	—	2510	5140	—

—=not measured.

chain) the weaker is the binding (compare the complexation constants K for chloride: **7a** (3480 M^{-1}), **7b** (1900 M^{-1}), **7c** (1790 M^{-1})). The comparison of **7a** and **7d** shows that thioureido derivative is slightly worse receptor for chloride if compared with the corresponding thiacalixarene bearing ureido functions. On the other hand, both thiacalix[4]arene receptors **7a** and **7d** exhibit higher complexation abilities for chloride than classical calix[4]arene derivative **7e**, while the situation with binding of cyanide anion is just reversed.

The relationship between the number of hydrogen bonds and the strength of anion complexation can be evaluated by comparing the binding affinity of **7a** ($K_{Cl}=3480\ M^{-1}$) with that of model derivative **9** ($K_{Cl}=220\ M^{-1}$) possessing only two thiourea moieties. The considerable difference (15×) in the complexation constants clearly demonstrates the importance of multiple hydrogen bonds and preorganisation for efficient anion binding.

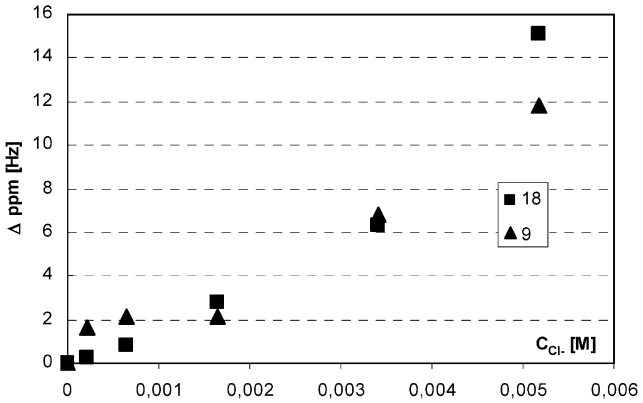


Figure 4. Complexation induced ^{1}H NMR chemical shifts in **7a**/Kobayashi agent system after addition of Bu_4NCl (300 MHz, $CDCl_3$–CD_3CN=4:1 v/v), for numbering see Figure 1.

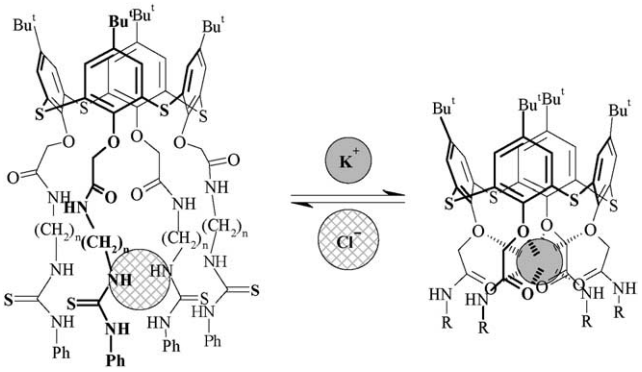


Figure 5. Competitive cation/anion complexation in derivative **7a**.

corresponding derivatives bearing four ureido or thioureido functions on the lower rim. The NMR titrations revealed that these compounds can interact with anions in apolar solvents via hydrogen bonding interactions and represent the first example of anion receptors in the thiacalixarene series.

3. Experimental

3.1. General

Melting points were determined on a Boetius block (Carl Zeiss Jena, Germany) and are not corrected. The IR spectra were measured on an FT-IR spectrometer Nicolet 740 in $CHCl_3$ and/or in KBr. ^{1}H NMR spectra were recorded on a Varian Gemini 300 spectrometer. Dichloromethane and CCl_4 used for the reaction were dried with CaH_2 and P_2O_5, respectively, and stored over molecular sieves. The purity of the substances and the course of reactions was monitored by TLC using TLC aluminium sheets with Silica gel 60 F_{254} (Merck). Preparative TLC chromatography was carried out on 20×20 cm glass plates covered by Silica gel 60 GF_{254} (Merck).

Starting esters **3a** (75%), **4a** (77%), and **8a** were prepared according to procedures known[20] by the reaction of **1** or **2** with ethyl bromoacetate in boiling acetone in the presence of Na_2CO_3 or Cs_2CO_3.

3.1.1. Preparation of acyl chlorides. *Synthesis of 5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis[(chlorocarbonyl)methoxy]-thiacalix[4]arene* (**3c**). Tetraacid **3b** (0.4 g, 0.42 mmol) was dissolved in anhydrous tetrachloromethane (20 ml) and oxalyl chloride (3 ml, 0.034 mol) was added. The reaction mixture was refluxed for 3 h and the volatile part of the reaction was distilled off. Fresh tetrachloromethane (5 ml) was then added and the distillation was repeated under reduced pressure. The product was immediately used in the next step.

Synthesis of 5,11,17,23-tetra-tert-butyl-25,26,27,28-[(chlorocarbonyl)methoxy]calix[4]arene (**4c**). Calixarene **4b** (0.4 g, 0.45 mmol) was reacted with oxalyl chloride (3 ml, 0.035 ml) following the same procedure as described above for **3c**. The product was obtained quantitatively, and was used immediately in the next step.

3.1.2. Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis[((*N*-2-aminoethyl)aminocarbonyl)-methoxy]thiacalix[4]arene (5). A solution of tetraester **3a** (1.1 g, 1.04 mmol) in 5 ml of absolute THF was added to 40 ml of ethylene diamine (598 mmol) and the mixture was stirred for four days at rt. The remaining ethylene diamine was distilled off at a reduced pressure, the residue was suspended in water, and the precipitate was filtered off. The crude product (0.92 g) was used without further purification in the next step. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.33 (broad peak, 4H, NH), 8.10 (b.s., 4H, NH), 7.34 (s, 8H, H-arom), 4.88 (s, 8H, O–*CH_2*–CO–), 3.43 (m, 8H, –NH–*CH_2*–CH_2–NH_2), 2.92 (m, 8H, NH–CH_2–*CH_2*–NH_2), 1.12 (s, 36H, Bu^t).

3.1.3. Synthesis of thioureas. *N-(2-Aminoethyl)-N′-phenylthiourea* (**6a**). Phenyl isothiocyanate (2.4 ml, 0.02 mol) in 5 ml of diethyl ether was added dropwise to the solution of 1.2 ml of ethylene-1,2-diamine (0.02 mol) in 30 ml of isopropyl alcohol over a period of 40 min. The reaction mixture was then stirred for 2 h at rt and quenched by addition of 80 ml of diluted HCl (40:1). The solvents were evaporated, the residue was suspended in hot water and the resulting precipitate was filtered off. The filtrate was basified by the addition of solid NaOH, and the product (1.8 g, 46%) crystallised in the form of white crystals. Mp: 135–136 °C (lit.[22] 135–137 °C). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 7.43 (t, 2H, J=7.7 Hz, H-arom), 7.28 (m, 3H, H-arom), 6.75 (b.s., 2H, NH) 3.67 (m, 2H, NH–CH_2–*CH_2*–NH), 2.92 (t, 2H, J=5.8 Hz, NH–*CH_2*–CH_2–NH).

N-(3-Aminopropyl)-N′-phenylthiourea (**6b**). Phenyl isothiocyanate (2.4 ml, 0.02 mol) in diethyl ether (5 ml) was added dropwise to the solution of 1.7 ml (0.02 mol) of propan-1,3-diamine in 30 ml of isopropyl alcohol during 40 min. The reaction mixture was stirred for 2 h at rt and quenched by addition of 80 ml of diluted HCl (40:1). The solvents were evaporated, the residue was suspended in hot water and the resulting precipitate was filtered off. The filtrate was basified by NaOH to approx. pH=10. After standing at rt the product crystallised to give 1.23 g of white crystals (30%). Mp: 103–105 °C (lit.[23] 106–107 °C).^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 7.77 (b.s., 1H, NH), 7.67 (b.s., 1H, NH), 7.38 (t, 2H, J=7.4 Hz, H-arom), 7.24 (d, 3H, J=6.6 Hz, H-arom), 3.74 (m, 2H, NH–*CH_2*–CH_2–CH_2–NH_2), 2.80 (m, 2H, NH–CH_2–CH_2–*CH_2*–NH_2), 1.66 (m, 2H, NH–CH_2–*CH_2*–CH_2–NH_2), 1.10 (b.s., 2H, NH_2).

N-(6-aminohexyl)-N′-phenylthiourea (**6c**). Phenyl isothiocyanate, 2.4 ml (0.02 mol) in diethyl ether (5 ml) was added dropwise to the solution of 2.32 ml (0.02 mol) hexane-1,6-diamine in 30 ml of isopropyl alcohol during 40 min. After addition of all the isothiocyanate, the reaction mixture was stirred for 2 h at rt and quenched with 80 ml of dilute HCl (40:1). The solvents were evaporated, the residue was suspended in hot water and the resulting solid was filtered off. The filtrate was basified by NaOH to pH=10 and the product crystallised from water to give 0.84 g of colourless crystals (17%). Mp: 90–92 °C (lit.[22] 89–92 °C. ^{1}H NMR ($CDCl_3$, 300 Hz) δ (ppm): 7.73 (b.s., 1H, NH), 7.44 (t, 2H, J=7.4 Hz, H-arom), 7.31 (t, 1H, J=7.7 Hz, H-arom), 7.19 (d, 2H, J=7.1 Hz, H-arom), 6.03 (b.s., 1H, NH), 3.62 (m,

2H, –NH–CH_2–CH_2–CH_2–), 2.66 (m, 2H, –CH_2–CH_2–NH_2), 1.57 (m, 2H, NH–CH_2–CH_2–CH_2–), 1.42 (m, 2H, –CH_2–CH_2–CH_2–NH_2), 1.32 (m, 4H, –NH–CH_2–CH_2–CH_2–CH_2–CH_2–CH_2–NH_2), 1.02 (b.s., 4H, NH_2).

3.1.4. Synthesis of receptors 7a–7e. *Receptor* **7a**. A solution of acyl chloride **3c** (0.23 g, 0.21 mmol) in 10 ml of absolute THF was added dropwise to a stirred solution of *N*-(2-aminoethyl)-*N′*-phenylthiourea (0.5 g, 2.56 mmol) in THF (10 ml) under the nitrogen atmosphere. Triethylamine (0.4 ml) was then added and the mixture was stirred for three days at rt. Reaction mixture was quenched by addition of 1 M aqueous HCl and the product was extracted with chloroform. The organic layer was dried on $MgSO_4$, evaporated to dryness and the solid residue was purified by preparative TLC (petroleum ether–acetone=2:1) to give 80 mg of title compound (23%) as a white solid. Mp: 142–146 °C. ^{1}H NMR ($CDCl_3$–CD_3CN=4:1, 300 MHz) δ (ppm): 8.46 (s, 4H, –NH), 8.30 (b.s., 4H, –NH), 7.35 (s, 8H, H-arom), 7.32 (d, 8H, J=7.7 Hz, H-arom), 7.30 (t, 8H, J=7.8 Hz, H-arom), 7.23 (b.s., 4H, –CH_2–CO*NH*–), 7.15 (t, 4H, J=7.1 Hz, H-arom), 4.87 (s, 8H, O–CH_2–CONH–), 3.80 (m, 8H, –NH–CH_2–CH_2–NH–), 3.54 (m, 8H, –NH–CH_2–CH_2–NH–), 1.10 (s, 36H, Bu^t). IR ($CHCl_3$) ν_{max} (cm^{-1}): 1663 (CO), 3306 (NH). MS-ES *m/z* (rel. int.) 853.10 $[M+2Na]^{2+}$ (33), 1683.27 $[M+Na]^+$ (52). EA calcd for $C_{84}H_{100}N_{12}O_8S_8$: C, 60.69; H, 6.06; N, 10.11%. Found: C, 60.23; H, 6.21; N, 10.01%.[24]

Receptor **7b**. Triethylamine (0.4 ml) was added to the solution of *N*-3-aminopropyl-*N′*-phenylthiourea **6b** 0.53 g (2.5 mmol) in anhydrous THF (10 ml) under nitrogen atmosphere. Then the solution of acyl chloride **3c** (0.23 g, 0.21 mmol) in THF (10 ml) was added and the reaction mixture was stirred for five days at rt. An aqueous 1 M solution of HCl was added and the product was extracted with chloroform. The organic layer was dried over $MgSO_4$, evaporated to dryness, and the crude product was purified using the preparative TLC on silica gel (20×20 cm, chloroform–acetone=2:1). The title compound (0.08 g, 26%) was obtained as a white solid. Mp: 136–139 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.23 (b.s., 4H, NH), 7.97 (b.s., 4H, NH), 7.35 (m, 8H, H-arom), 7.33 (s, 8H, H-arom), 7.25 (m, 8H, H-arom), 7.20 (m, 4H, H-arom), 6.99 (b.s., 4H, NH), 4.79 (s, 8H, O–CH_2–CONH–), 3.62 (m, 8H, NH–CH_2–CH_2–CH_2–NH), 3.31 (m, 8H, NH–CH_2–CH_2–CH_2–NH), 1.81 (m, 8H, NH–CH_2–CH_2–CH_2–NH_2), 1.11 (s, 36H, Bu^t). IR ($CHCl_3$) ν_{max} (cm^{-1}): 1663 (C=O), 3317 (NH). MS-ESI *m/z* (rel int.) 881.63 $[M+2Na]^{2+}$ (66), 1740.28 $[M+Na]^+$ (100). EA calcd for $C_{88}H_{108}N_{12}O_8S_8$: C, 61.51; H, 6.33; N, 9.78%. Found: C, 61.13; H, 6.56; N, 9.84%.[24]

Receptor **7c**. *N*-6-Aminohexyl-*N′*-phenylthiourea **6c** (0.44 g, 1.753 mmol) was dissolved in anhydrous THF (10 ml) under nitrogen atmosphere and treated with triethylamine (0.3 ml) and the solution of **3c** (0.16 g, 0.14 mmol) in THF (5 ml) was added. The reaction mixture was then stirred for five days at rt and purified as described above for **7b** to give 0.062 g of product (22%) as a white solid. Mp: 96–99 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.06 (s, 4H, SH), 7.98 (b.s., 4H, NH), 7.36 (s, 8H, Ar-H), 7.36 (m, 8H, H-arom), 7.29 (m, 8H, H-arom), 7.19 (t, 4H, J=7.2 Hz, H-arom), 6.58 (b.s., 4H, NH), 4.79 (s, 8H, O–CH_2–CONH–), 3.59 (m, 8H, NH–CH_2–$(CH)_5$–NH), 3.32 (m, 8H, NH–$(CH)_5$–CH_2–NH), 1.57 (m, 16H, NH–CH_2–CH_2–$(CH_2)_2$–CH_2–CH_2–NH), 1.34 (m, 16H, NH–$(CH_2)_2$–CH_2–CH_2–$(CH_2)_2$–NH), 1.12 (s, 36H, Bu^t). IR ($CHCl_3$) ν_{max} (cm^{-1}): 1665 (CO), 3326 (NH). MS-ESI *m/z* (rel. int.) 965.67 $[M+2Na]^{2+}$ (98), 1908.2 $[M+Na]^+$ (100). EA calcd for $C_{100}H_{132}N_{12}O_8S_8$: C, 63.66; H, 7.05; N, 8.91%. Found: C, 62.93; H, 7.11; N, 8.71%.[24]

Receptor **7d**. A solution of phenyl isocyanate (0.72 ml, 6.6 mmol) in ether (10 ml) was added to derivative **5** (0.92 g, 0.82 mmol) dissolved in 15 ml of isopropyl alcohol. The reaction mixture was stirred at rt for 2 h, then 20 ml of water was added and the product was extracted with chloroform. The organic layer was dried over $MgSO_4$, evaporated to dryness and the residue was purified using column chromatography on silica gel ($CHCl_3$–ethyl acetate=100:1) to yield 0.108 g of the product (8% overall from **3a**) as a yellowish solid. Mp: 162–166 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm): 8.51 (b.s., 8H, 2NH), 7.37 (s, 8H, H-arom), 7.34 (d, 8H, J=7.1 Hz, H-arom), 7.18 (t, 8H, J=7.2 Hz, H-arom), 6.86 (t, 4H, J=7.0 Hz, H-arom), 6.27 (t, 4H, J=4.9 Hz, NH), 4.84 (s, 8H, O–CH_2–CONH–), 3.29 (m, 8H, NH–CH_2–CH_2–NH), 3.22 (m, 8H, NH–CH_2–CH_2–NH), 1.06 (s, 36H, Bu^t). IR ($CHCl_3$) ν_{max} (cm^{-1}): 1659 (CO), 3321 (NH). MS-ESI *m/z* 1619.3 $[M+Na]^+$. EA calcd for $C_{84}H_{100}N_{12}O_{12}S_4$: C, 63.13; H, 6.31; N, 10.52%. Found: C, 62.63; H, 6.02; N, 10.11%.[24]

Receptor **7e**. *N*−2-aminoethyl-*N′*-phenylthiourea **6a** (0.7 g, 0.0035 mol) and 0.4 ml of triethylamine were dissolved in anhydrous THF (10 ml) under a nitrogen atmosphere. A solution of acyl chloride **4c** (0.43 g, 0.45 mmol) in 10 ml of anhydrous THF was added and the mixture was stirred for three days at rt. The reaction mixture was then quenched by aqueous 1 M HCl (10 ml) and the product was extracted to chloroform. The organic layer was dried over $MgSO_4$, solvent was removed under a reduced pressure, and the residue was purified by preparative TLC ($CHCl_3$–methanol=10:1) to yield 50 mg (7%) of product as a white solid. Mp: 136–142 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.35 (b.s., 4H, NH); 8.20 (b.s., 4H, NH); 7.28–7.19 (m, 24H, H-arom, NH); 6.77 (s, 8H, H-arom); 4.52 (s, 8H, O–CH_2–CO); 4.43 (d, 4H, J=13.2 Hz, Ar-CH_2-Ar ax.); 3.77 (m, 8H, –CH_2–CH_2–); 3.52 (m, 8H, –CH_2–CH_2–); 3.23 (d, 4H, J=13.2 Hz, Ar-CH_2-Ar eq.); 1.06 (s, 36H, Bu^t). MS-ESI *m/z* (rel. int.) 817.64 $[M+2Na]^{2+}$ (65), 1611.4 $[M+Na]^+$ (100). EA calcd for $C_{88}H_{108}N_{12}O_8S_4$: C, 66.47; H, 6.85; N, 10.57%. Found: C, 65.98; H, 6.88; N, 10.17%.[24]

3.1.5. Synthesis of receptor 9. Di-acid **8b** (0.117 g, 0.14 mmol) was dissolved in 20 ml of dry DMF under the nitrogen atmosphere, the *N*,*N′*-carbonyl diimidazole (0.05 g, 0.294 mmol) was added and the mixture was stirred for 1 h at rt. A solution of *N*-(2-aminoethyl)-*N′*-phenylthiourea **6a** (0.11 g, 0.56 mmol) in DMF was added and the mixture was heated to 70 °C overnight. The solvents were distilled off under a reduced pressure and the remaining solid was purified by the preparative TLC on silica gel ($CHCl_3$–acetone=10:1) to give 90 mg of product (54%) as a white solid. Mp: 181–183 °C. ^{1}H NMR ($CDCl_3$–CD_3CN=4:1) δ (ppm): 8.45 (s, 2H, OH), 8.27 (b.s., 2H, NH), 8.12 (b.s., 2H, NH), 7.53 (s, 4H, H-arom), 7.16 (s, 4H,

H-arom), 7.12 (m, 8H, H-arom), 6.98 (m, 2H, H-arom), 6.91 (b.s., 2H, NH), 4.77 (s, 4H, O–CH_2–CONH–), 3.76 (m, 4H, NH–CH_2–CH_2–NH), 3.56 (m, 4H, NH–CH_2–CH_2–NH), 1.17 (s, 18H, Bu^t), 0.83 (s, 18H, Bu^t). IR ($CHCl_3$) ν_{max} (cm^{-1}): 1671 (CO), 3340 (NH). MS ES *m/z* (rel. int.) 1191.09 $[M+H]^+$ (22), 1213.1 $[M+Na]^+$ (100). EA calcd for $C_{62}H_{74}N_6O_6S_6$: C, 62.49; H, 6.26; N, 7.05%. Found: C, 61.88; H, 6.31; N, 6.87%.

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24. The EA usually resulted in C values about 1 to 2% lower than the calculated values. This fact is well documented in calixarene chemistry and there are two widely accepted explanations: (i) cavity of calixarenes contains the molecules of solvents/reagents, which are extremely difficult to eliminate; (ii) the incomplete combustion of these high-melting compounds under the standardized conditions of the elemental analysis. We believe that the structures of the calixarenes are sufficiently documented by the spectral evidence.