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Systematic approach to new ligands for anion recognition based on ureido-calix[4]arenes†

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Mono, di-, tri- and tetraureido-calix[4]arenes in the *cone*, *partial cone* and 1,3-*alternate* conformations have been synthesised and their complexation ability towards selected anions has been studied. The structure–anion complexation ability relationship has been systematically monitored. A new type of very efficient ligands based on diureido-calix[4]arene in a 1,3-*alternate* conformation with pronounced bonding ability towards carboxylates was designed.

Introduction

The complexation of anionic species continues to attract the attention of the chemical community as witnessed by numerous reviews published recently.[1] The importance of anions in biological systems is well recognised. The same is true for the role of anions in chemical processes and environmental pollution. Given their importance, there has obviously been much effort expended in the design of anion complexing ligands. The main strategies have traditionally focused on cationic, polyammonium, quanidinium, quaternary ammonium, porphyrin-based ligands, and a number of Lewis-acid containing ligands. Neutral organic ligands for anion binding *via* favourable hydrogen bonding have also been thoroughly studied and recently reviewed.[2] Calixarenes are extremely versatile macrocyclic compounds with well developed chemistry and abundant literature.[3] Many neutral organic ligands based on the calixarene macrocyclic skeleton have been reported in literature. For this work the most relevant are calixarene-based neutral ligands having no metal ion inherently bound. A number of such ligands have been used for binding of anions[4] or cation–anion couples.[5] Our own research has been oriented to anion recognition using simple (hetero)aromatic amides,[6a–c] ureas[6d] or calixarene-based ligands.[6e–h] Working with the calixarene based ligands for anions we have found that bis-(phenyluredio)-calix[4]arene in cone conformation is able to bind benzoate with surprisingly high selectivity. Moreover, tetrakis(phenylureido)-calix[4]arene in 1,3-alternate conformation has been found to bind anions with negative allosteric effect.[6e] We have also examined calixarene based cages[6f] as well as calixarene–porphyrin based ligands.[6g] The unexpected results[6e] mentioned above have prompted us to study ureido-calix[4]arenes systematically. Here we report, on the synthesis, binding ability and selectivity profile of several ureido-calix[4]arenes with one to four urea units appended to the calix[4]arene skeleton in *cone*, *partial-cone* and 1,3-*alternate* conformations.

Results and discussion

Design

Thirteen ureido-calix[4]arenes have been chosen for the study of structure–anion binding ability relationship (Fig. 1). Compounds **1**, **10** and **14** have been already mentioned.[6e] Monoureido derivative **2** is used in comparison with **1** and **4** to study the cooperation of two and three ureido groups. Accordingly, comparison of **1**, and **3** would tell us more about the role of proximity in cooperative action of two ureido groups. The role of the substituent on the other side of the urea unit (apart from the calixarene moiety) can be easily evaluated by comparison of **1** (phenyl), **5** (benzyl), **6** (cyclohexyl) and **8** (1-(1-naphthylethyl)). The role of lower rim substitution can be illustrated by comparison of ligands **1** (tetraalkoxy) and **7** (distal-dihydroxydialkoxy). All the above mentioned compounds have been built on the calix[4]arene skeleton in *cone* conformation. The role of the calixarene conformation can be assessed by comparison of **1** (*cone*), **9** (*partial cone*), **10** (1,3-*alternate-tetrasubstituted*) and **13** (1,3-*alternate-disubstituted*) for phenylureido compounds or **5** (*cone*) and **11** (1,3-*alternate-tetrasubstituted*), **8** (*cone*), **12** (1,3-*alternate-tetrasubstituted*). The unique role of 1,3-*alternate* calix[4]arene skeleton flexibility can be easily estimated by comparison of tetrasubstituted **10** and disubstituted **13**.

Synthesis

The synthesis of compounds **1**, **10** and **14** has been mentioned previously.[6e] In general, the synthesis of ligands described is straightforward following the traditional sequence: calix[4]arene—nitration to nitrocalix[4]arene—reduction to aminocalix[4]arene—reaction with aryl isocyanate to form ureido-calix[4]arene. All known intermediates we have used in our synthetic procedures are cited in the Experimental section. Nitration of calix[*n*]arenes is a well described procedure. Nevertheless, we have had to develop

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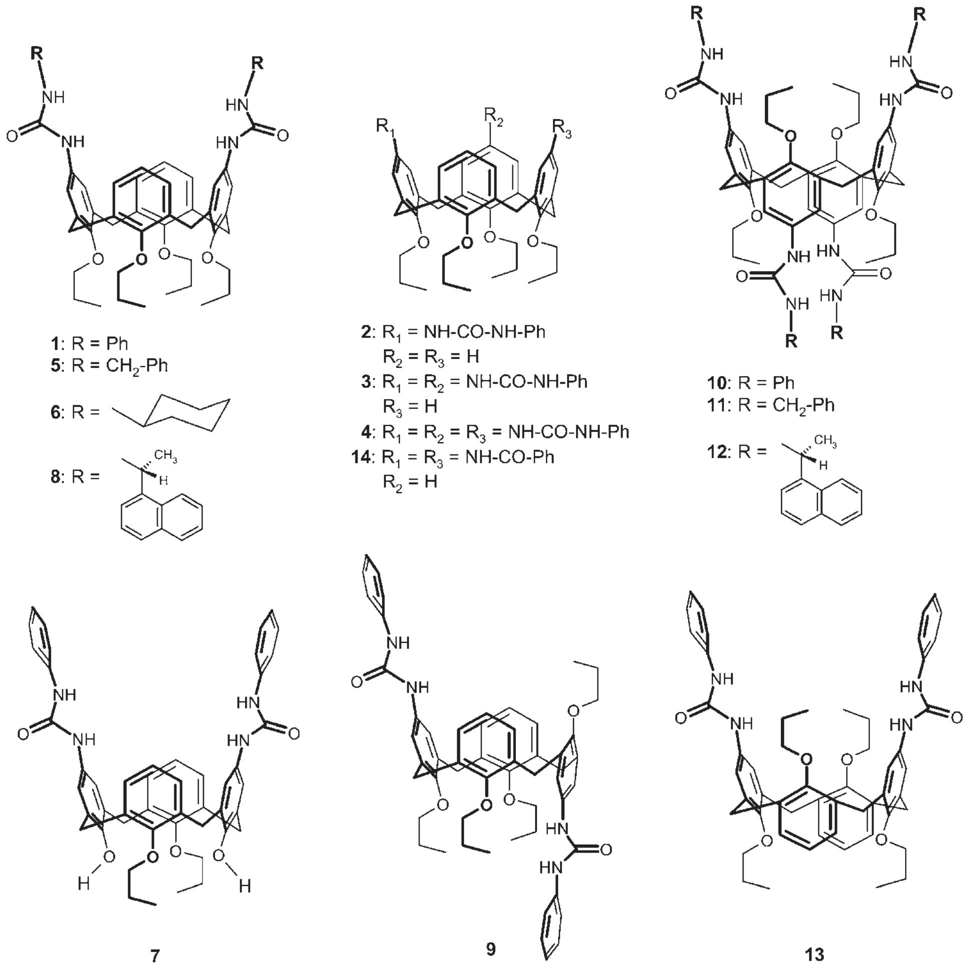
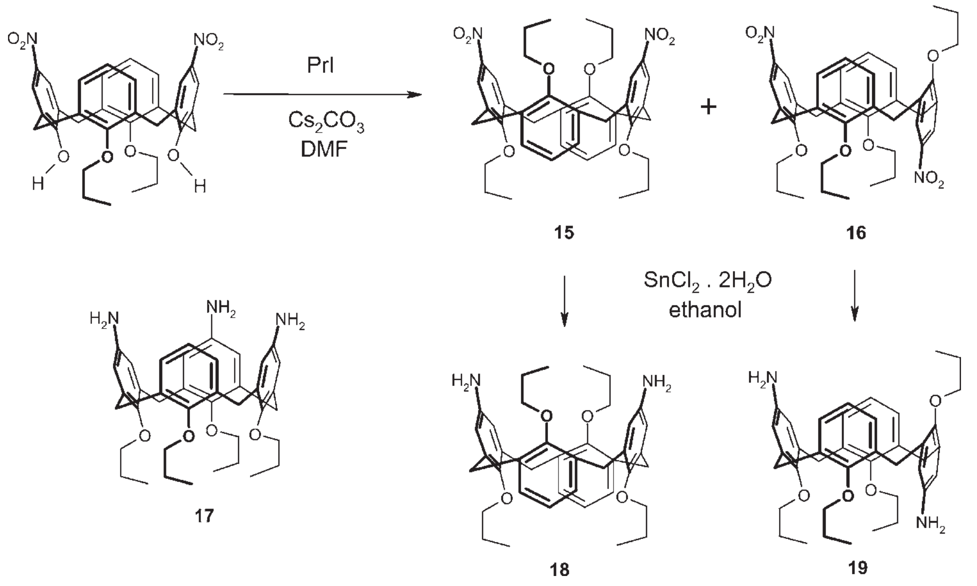


Fig. 1 Prepared urea derivatives of calix[4]arene.

a method for the synthesis of 5,17-dinitro-25,26,27,28-tetrapropoxycalix[4]arene in both 1,3-*alternate* (**15**) and *partial cone* (**16**) conformations (Scheme 1). In this context we have used the alkylation of 5,17-dinitro-25,27-dipropoxycalix[4]arene-26,28-diol[7] with propyl iodide templated by caesium carbonate in DMF. This procedure led to a mixture of **15** and **16** in 26 and 67% yields,



Scheme 1 Preparation of new nitro and amino derivatives.

respectively. Separation of these conformers can be achieved only by column chromatography which makes the procedure somewhat laborious for pure **15** despite the great difference in chromatographic mobility of both compounds ($R_F^{\mathbf{15}}$ = 0.4 and $R_F^{\mathbf{16}}$ = 0.9). There are several methods for preparation of amino-substituted calix[4]arenes described in literature. In our hands the reduction by $SnCl_2$ dihydrate[7b,8,9] was found to give the best results in terms of yield and purity of sometimes unstable amino-calix[4]arenes. Thus, we have prepared all previously described amino-calix[4]arenes, namely 5-amino-25,26,27,28-tetrapropoxycalix[4]arene (*cone*),[9] 5,11-diamino-25,26,27,28-tetrapropoxycalix[4]arene (*cone*),[9,10] 5,17-diamino-25,26,27,28-tetrapropoxycalix[4]arene (*cone*),[9,10] 5,17-diamino-25,27-dipropoxycalix[4]arene-26,28-diol (*cone*),[11] 5,11,17,23-tetraamino-25,26,27,28-tetrapropoxycalix[4]arene (*cone*),[12] 5,11,17,23-tetraamino-25,26,27,28-tetrapropoxycalix[4]arene (1,3-*alternate*),[9] as well as new amino-calix[4]arenes, namely 5,11,17-triamino-25,26,27,28-tetrapropoxycalix[4]arene (*cone*) (**17**), 5,17-diamino-25,26,27,28-tetrapropoxycalix[4]arene (1,3-*alternate*) (**18**), 5,17-diamino-25,26,27,28-tetrapropoxycalix[4]arene (*partial cone*) (**19**), in excellent yields (Scheme 1). The synthesis of ureas was performed using a standard reaction protocol[13] with commercially available isocyanates.

Complexation

The complexation ability of the prepared compounds have been screened by standard ^{1}H NMR titration experiment using a constant calixarene concentration (0.5–2.0 mM) and increasing concentration of appropriate anion to obtain different host : guest ratios (0.1–20 : 1).[6e] In order to compare all data obtained we have used two solvents, namely A: $CDCl_3$–CD_3CN = 4 : 1 and B: $CDCl_3$–CD_3SOCD_3 = 4 : 1, both v/v. Compounds **1** and **10** have been taken as references and their complexation ability have been measured in both solvent systems. The results obtained are summarised in Tables 1–3.

In all but one case only formation of 1 : 1 complexes were observed (Job plots)[14] what means that in both solvents two ureas positioned on one side of ligands **1** and **10** cooperate in binding of one anion regardless its size, shape and solvation. The only exception is compound **9** where cooperative action of both ureido groups is not possible as witnessed by its X-ray structure (see later). The data for ligands **1** and **10** in solvent A have already been discussed.[6e] Anyhow, the comparison of complexation constants in both solvent systems requires several comments. A negative allosteric effect already observed[6e] in solvent A is retained also in solvent B. The diameter of the halide anions is reflected by complexation ability only for the conformationaly rigid ligand **10**. The extraordinary preference of ligand **1** for benzoate is not retained in solvent B that can be explained by the loss of the cooperative action of both hydrogen bonding and π–π stacking interaction due to better solvation of aromatic moieties of both ligand and anion by DMSO.[15] This is reflected by the ratio of complexation constants of benzoate/acetate by ligand **1** that has changed from almost 41 in solvent A to less than 4 in solvent B. This phenomenon deserves further attention and is under study in our laboratory.

The cooperative action of ureido moieties on the same side of calix[4]arene skeleton in the *cone* conformation can be illustrated by examining the complexation ability of ligands **2**, **1** and **4** having one, two and three ureas on the same side of calixarene skeleton. Disubstituted ligand **3** was prepared to illustrate the role of the substitution pattern of the upper rim of the calix[4]arene skeleton in the binding process (proximal **3** *vs*. distal **1**). The data obtained are summarised in Table 1.

Well known dimerisation phenomena have been described for the upper-rim tetraurea derivatives of calix[4]arenes.[16] These compounds form capsules due to their multiple hydrogen bonds in non-competitive solvents such as chloroform or dichloromethane. All ureido derivatives, with the exception of **3** and **4**, exhibit clear and concentration-independent ^{1}H NMR spectra. Triureido derivative **4** shows a strong concentration dependence in solvent A (see Fig. 2). Unfortunately, all signals are very broad and the self-aggregation cannot be determined quantitatively. Fig. 3 shows the changes in spectra of compound **4** after addition of 10% (v/v) of $(CD_3)_2SO$. The broad and irresolvable signals changed into a clear spectrum. The same situation has also been found in the case of proximal diureido derivative **3** (Fig. 4). It seems that the self-aggregation process is typical for calixarenes bearing ureido groups on neighbouring aromatic units (proximal arrangement). Consequently, the ^{1}H NMR titrations of **3** and **4** were performed in solvent B, where self-aggregation is not present at all.

The following conclusions can be drawn from Tables 1 and 2. The cooperation of both urea moieties in **1** (distal) is clearly indicated by comparison with model compound **2** having only one urea unit. Synchronous binding by both ureas is responsible for enhancement of complex stability by more than two orders

Table 1 Complexation constants of *cone* ligands **1–4** and **7** towards selected anions (solvent A: $CDCl_3$–CD_3CN = 4 : 1 and B: $CDCl_3$–CD_3SOCD_3 = 4 : 1, v/v, 25 °C, 300 MHz)

K_C/M^{-1}						
	2	**1**		**3**	4	**7**
Anion	A	A[6e]	B	B	B	B
Cl^-	390 ± 20	4700 ± 490	60 ± 6	160 ± 70	240 ± 90	60 ± 10
Br^-	110 ± 20	1400 ± 160	15 ± 5	80 ± 10	180 ± 30	20 ± 10
I^-	40 ± 7	710 ± 190	n.c.[a]	n.c.[a]	n.c.[a]	n.c.[a]
$H_2PO_4^-$	900 ± 130	2300 ± 480	660 ± 50	350 ± 120	—[b]	420 ± 20
$MeCO_2^-$	3000 ± 300	4000 ± 1100	520 ± 80	1200 ± 120	880 ± 190	250 ± 20
$PhCO_2^-$	1500 ± 300	160 000 ± 45 000	2100 ± 190	1300 ± 120	1700 ± 600	130 ± 10

[a] No complexation observed (CIS < 5 Hz). [b] Not determined stoichiometry.

Table 2 Complexation constants of ligands **1**, **5**, **6**, **8** (*cone*) and **9** (*partial cone*) towards selected anions (solvent: $CDCl_3$–CD_3CN = 4 : 1, v/v, 25 °C, 300 MHz)

K_C/M^{-1}					
Anion	**1**[6e]	**5**	**6**	**8**	**9**
Cl^-	4700 ± 490	410 ± 50	1300 ± 210	590 ± 40	1100 ± 160
Br^-	1400 ± 160	170 ± 30	170 ± 60	100 ± 20	290 ± 60
I^-	710 ± 190	130 ± 40	60 ± 20	15 ± 5	130 ± 50
$H_2PO_4^-$	2300 ± 480	1100 ± 200	530 ± 260	770 ± 270	—[a]
$MeCO_2^-$	4000 ± 1100	5800 ± 1500	1400 ± 190	90 ± 10	2000 ± 280
$PhCO_2^-$	160 000 ± 45 000	6200 ± 820	1700 ± 110	8400 ± 3400	1700 ± 200

[a] Undetermined stoichiometry.

Table 3 Complexation constants of 1,3-*alternate* ligands **10–13** towards selected anions (solvent A: $CDCl_3$–CD_3CN = 4 : 1 and B: $CDCl_3$–CD_3SOCD_3 = 4 : 1, v/v, 25 °C, 300 MHz)

K_C/M^{-1}						
	11	**10**		**12**	**13**	
Anion	A	A[6e]	B	B	A	B
Cl–	800 ± 220	4700 ± 190	140 ± 20	60 ± 20	36 000 ± 13 000	690 ± 170
Br–	790 ± 390	1500 ± 90	80 ± 20	20 ± 10	2400 ± 570	580 ± 270
I–	1800 ± 550	570 ± 90	42 ± 10	n.c. [a]	840 ± 570	n.c. [a]
$H_2PO_4^-$	3200 ± 1000	2700 ± 300	200 ± 60	250 ± 40	6900 ± 960	4200 ± 1000
$MeCO_2^-$	1400 ± 310	2200 ± 200	620 ± 300	100 ± 20	> 1 000 000	920 ± 320
$PhCO_2^-$	2100 ± 300	1800 ± 700	750 ± 360	50 ± 20	> 1 000 000	3500 ± 1800

[a] No complexation observed (CIS < 5 Hz).

of magnitude for benzoate, and around one order of magnitude for halides. The comparison of distal and proximal disubstituted ligands **3** and **1** revealed that a proximal substitution pattern is better for chloride, dihydrogen phosphate and acetate whereas distal is by far better for benzoate and larger spherical halides. Using 4-nitrophenylurea in the same positions, an unusual behaviour has been observed for proximal ligands of type **3**. In this case the complexation event has been found to promote dimerisation of ligands around the central anion to form the complexes with 2 : 1 (calix : anion) stoichiometry.[17] Ligand **4** with three ureas is even better for chloride and acetate but less suitable for dihydrogen phosphate and benzoate. The profound difference between acetate and benzoate can be explained in terms of a much smaller steric demand of the former and absence of additional stacking interaction proven for later. In general, smaller and compact anions are better bound by two ureas in proximal position in contrast with larger and aromatic anions that are better bound with two distal ureas. The third urea did not bring much efficiency (max. 50%) in binding of any anion studied. Considering their rather demanding synthesis, the trisubstituted calixarenes did not seem to be prospective candidates for further ligand development.

The role of substituent R in ligands **1**, **5**, **6** and **8** can be assessed by inspecting the data collected in Table 2. Comparison of receptors **1** (aromatic ring directly connected to urea) and **5** (benzyl derivative having the phenyl ring "isolated" by one CH_2 group from the urea moiety) indicates the role of the substitution. Generally, two factors are in play simultaneously: (i) the loss of interaction between *ortho*-aromatic hydrogens and anion in **5** (well documented for **1** by > 0.5 ppm shift of signals of these protons during the titration experiment), (ii) the loss of rigidity (and/or directionality) of aromatic units in **5** due to the CH_2 spacer leading to possible steric hindrance in the urea surroundings. As a result, a substantial decrease of complexation constant is observed in $CDCl_3$–CD_3CN solution for all anions except for acetate (see Table 2). A similar situation can be seen in compound **6** where the cyclohexyl unit is connected to the urea nitrogen *via* an sp^3 carbon (most probably *via* an equatorial bond) giving higher mobility to the cyclohexyl moiety compared to phenyl. As a result, all complexation constants are much lower than those for receptor **1**. Chiral ligand **8** can be seen as a combination of both **5** and **6** as the urea substituent is of benzyl type being attached by a tertiary carbon atom. These two factors result in severe loss of binding ability towards all anions. On the other hand, the absolute value of the complexation constant for benzoate (8400 ± 340 M^{-1}) indicates that this type of receptor can be used for aromatic carboxylate recognition.

Very similar reasoning can be applied to ligands with the calix[4]arene skeleton in a 1,3-*alternate* conformation. Ligands **10**, **11** and **12** illustrate the situation by their complexation data as summarised in Table 3.

Analogous behaviour was found for compounds with the calix[4]arene skeleton in 1,3-*alternate* conformation. Again, a severe decrease of complexation is seen for almost all cases going from aryl urea (**10**) to benzyl (**11**) or naphthylmethyl (**12**), except for acetate that is better bound by **10** and dihydrogen phosphate that is better bound by **12**. Tetrasubstituted ligands in a 1,3-*alternate* conformation showed a negative allosteric effect for all anions studied. Moreover, since

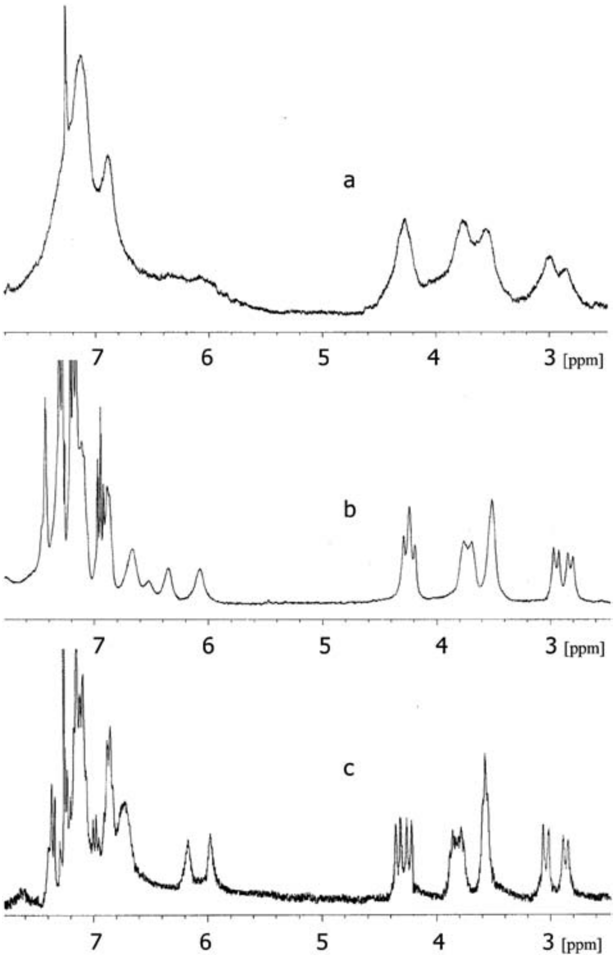


Fig. 2 Partial ^{1}H NMR spectra of derivative **4** ($CDCl_3$, 298 K) at various concentrations: (a) 1×10^{-3} M, (b) 6×10^{-4} M, (c) 3×10^{-4}.

their skeletons appear to be so rigid, ligands of this type did not seem to be good candidates for further structural tuning.

In order to learn more about the role of flexibility of the calix[4]arene skeleton in a 1,3-*alternate* conformation we decided to study analogous compounds having only one side of skeleton substituted with ureido functions. As we have shown tetrasubstituted receptors in a 1,3-*alternate* conformation behave as monotopic receptors and only one cavity is used for anion complexation. Hence, two ureido moieties can be omitted without influencing the binding efficiency. Furthermore, one can expect slightly higher flexibility of this type of receptor if compared with **10**. This should enable the binding site to adopt the most suitable conformation in terms of the induced fit principle.

Compound **13** is the first member of completely new ligand design with surprisingly enhanced ability for anion binding. The only difference, compared with receptor **10**, is that two additional ureido functions on the other side of the 1,3-*alternate* calix[4]arene skeleton were "deleted" from the molecule. Despite the fact that the structure difference is remote with respect to the ureido binding pocket, the change in binding ability is immediately apparent (see Table 3).

The effect of the number of urea units on the anion complexation can be demonstrated by comparison of the binding ability of diureido receptor **1** with that of model compound **2**.

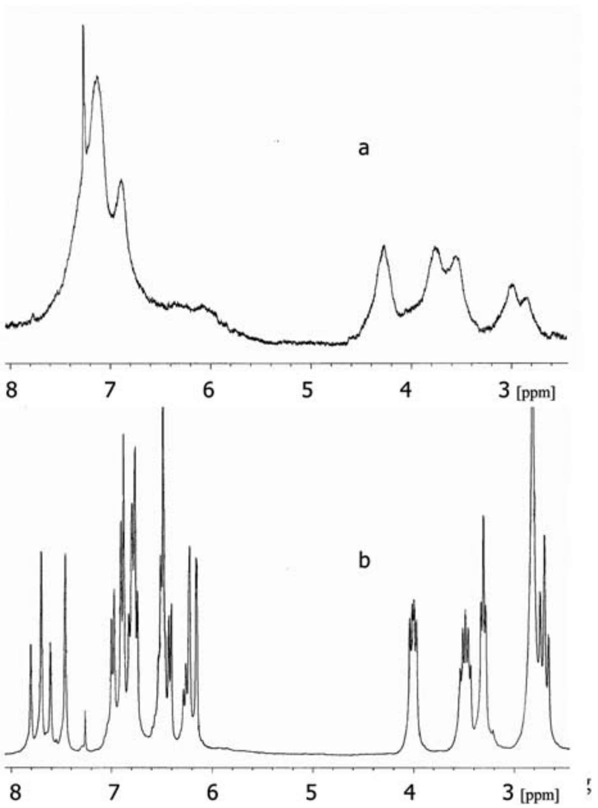


Fig. 3 Partial ^{1}H NMR spectra of compound **4** at 298 K: (a) in $CDCl_3$, (b) in $CDCl_3$–$(CD_3)_2SO$ = 10 : 1 v/v mixture.

Obviously, albeit both receptors are immobilised in the *cone* conformation, the derivative **1** exhibits much stronger complexation (K_{Cl} = 4.7×10^3 M^{-1}, K_{Br} = 1.4×10^3 M^{-1}) than calixarene **2** (K_{Cl} = 3.9×10^2 M^{-1}, K_{Br} = 1.1×10^2 M^{-1}) possessing only one urea unit. The difference of one order of

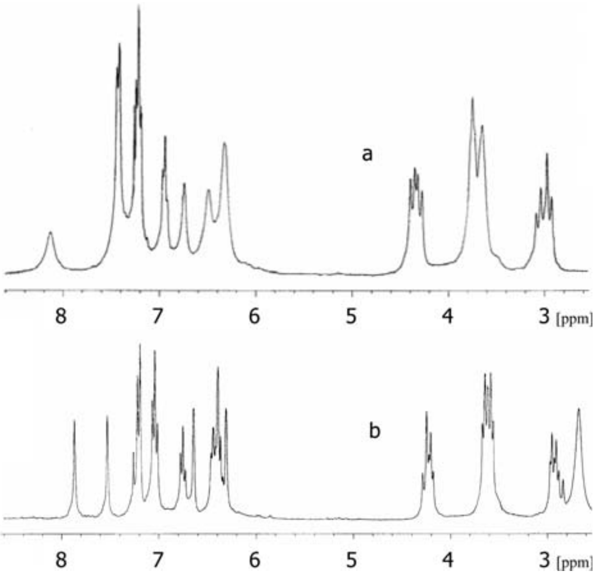


Fig. 4 Partial ^{1}H NMR spectra of derivative **3** at 298 K: (a) in $CDCl_3$, (b) $CDCl_3$–$(CD_3)_2SO$ = 10 : 1 v/v.

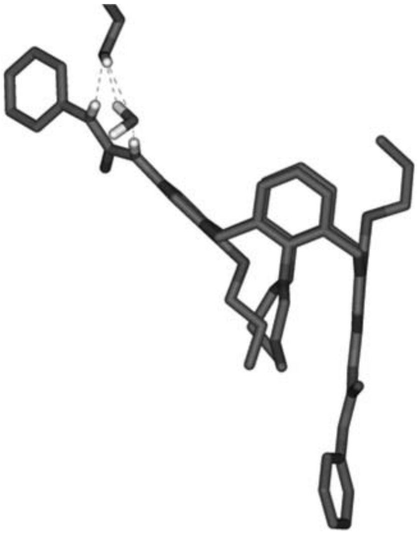


Fig. 5 X-Ray structure of the partial cone derivative **9**; hydrogen atoms are omitted for better clarity.

magnitude indicates the importance of a hydrogen bonding array for effective anion binding (cooperative effect).

Similar results were found for ligand **9** having two ureas attached to the calix[4]arene skeleton in the *partial cone* conformation. In this case, the substitution pattern prevents effective cooperative action of urea moieties. As a consequence, disubstituted *partial cone* compound **9** binds all anions studied in very similar manner as monosubstituted ligand **2**. On the other hand, the complexation data obtained for $H_2PO_4^-$ indicated that both urea moieties of calixarene **9** can also act separately leading to 2 : 1 (anion : ligand) complex stoichiometry.

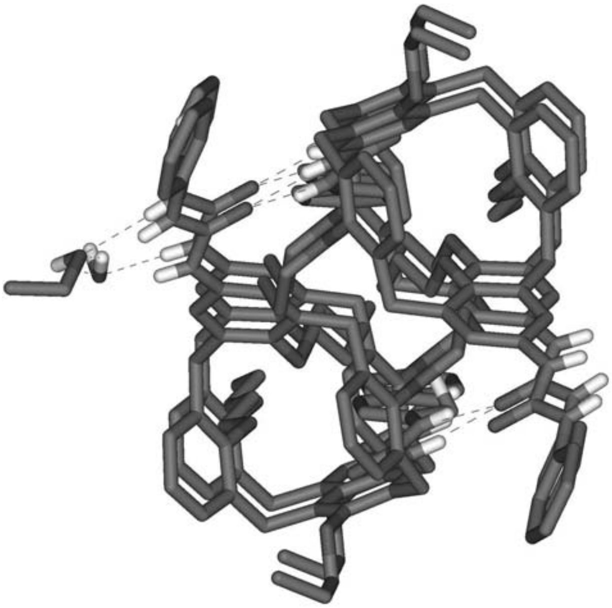


Fig. 6 Crystal packing of the *partial cone* derivative **9** showing hydrogen bonding interactions; hydrogen atoms are omitted for better clarity.

The solid-state structure of compound **9** was obtained by single-crystal X-ray crystallography. This calixarene formed a complex with water and ethanol molecules (Fig. 5) which crystallised in the orthorhombic system with three screw axes 2_1 perpendicular to each other. Consequently, the molecules form a helix in the crystal packing held together by hydrogen bonds between ureido groups of each calixarene (C=O and both NH-groups). This fact is clearly visible in the direction of the *b* axis (Fig. 6). Every two molecules overlap in this direction but are shifted to each other in the *b* direction by *b*/2 thus creating infinite channels (from top view). A water molecule forms a bridge between the helices and is bound in two ways to ureido units—to the carbonyl group of one molecule and on the opposite site to one of NH groups of other molecules. Ethanol (crystallisation solvent) is then connected *via* hydrogen bonds to the water molecule.

Conclusions

In conclusion, we have studied a number of ureido-calixarene-based neutral ligands with different number and spatial positions of ureido groups towards complexation of anions. This systematic study resulted in the structure of ligand **13** which is regarded as a new, very efficient scaffold that will be used for modular construction of anion receptors with the possibility to be extended to the recognition of chiral anions. We are currently working on this project.

Experimental

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. ^1H NMR spectra were recorded on a Varian Gemini 300 spectrometer, the temperature-dependant spectra were recorded on Bruker AMX3 400 and Bruker DRX 500 Avance spectrometers using tetramethylsilane as an internal standard. Dichloromethane used for the reaction was dried with CaH_2, and stored over molecular sieves. The purity of the substances and the courses of reactions were 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).

5,17-Bis(*N*′-phenylureido)-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) 1

To a stirred solution of 100 mg (0.16 mmol) of 5,17-diamino-24,25,26,27-tetrapropoxycalix[4]arene in 6 ml of dry dichloromethane 0.87 ml (8.0 mmol) of phenyl isocyanate was added. The mixture was stirred at room temperature for 12 h and poured into methanol to give 86 mg (63%) of compound **1** as a white precipitate, mp 266–268 °C (Found: C, 75.0; H, 6.9; N, 6.6. $C_{54}H_{60}N_4O_6$ requires: C 75.32; H 7.02; N 6.51%; M^+ 860.4). δ_H (300 MHz; $CDCl_3$; Me_4Si): 7.32 (4H, m, Ar-H), 7.25 (4H, d, *J* 7.7, Ar-H), 7.12 (4H, d, *J* 7.7, Ar-H), 7.04 (2H, t, *J* 6.8, Ar-H), 6.93 (2H, t, *J* 7.2, Ar-H), 6.00 (4H, s, Ar-H), 4.46 (4H, d, *J* 13.4, Ar–CH_2–Ar *ax*), 4.01 (4H, t, *J* 8.3, 2 × OCH_2), 3.67 (4H, t, *J* 6.6, 2 × OCH_2), 3.16 (4H, d, *J* 14.3, Ar–CH_2–Ar *eq*), 1.96–1.83 (8H, m, 4 × $\mathrm{OCH_2C}\mathit{H}_2$), 1.11 (6H, t, *J* 7.5, 2 × $\mathrm{CH_3}$), 0.87 (6H, t, *J* 7.5, 2 × $\mathrm{CH_3}$). $[\mathrm{M} + \mathrm{H}]^+$ 861.8.

5-(*N*′-Phenylureido)-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) 2

To a stirred mixture of 100 mg (0.16 mmol) of 5-amino-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) in 3 ml of dry dichloromethane 0.4 ml (3.2 mmol) of phenyl isocyanate was added. The mixture was stirred at room temperature for 12 h, poured into methanol, stirred for 30 min and evaporated to dryness. The residue was separated on 30 g of silica gel (petroleum ether–ethyl acetate 10 : 1) to yield 80 mg (67%) of compound **2** as a white powder, mp 137–140 °C (Found: C, 77.4; H, 7.4; N, 3.7. $\mathrm{C_{47}H_{54}N_2O_5}$ requires C 77.65; H 7.49; N 3.85%). δ_H (300 MHz; $\mathrm{CDCl_3}$; $\mathrm{Me_4Si}$): 7.30 (2H, d, *J* 7.7, Ar-H), 7.20 (2H, d, *J* 7.2, Ar-H), 7.06 (1H, t, *J* 7.7, Ar-H), 6.96–6.90 (4H, m, Ar-H), 6.81 (2H, d, *J* 7.2, Ar-H), 6.33–6.23 (3H, m, Ar-H), 6.26 (2H, s, Ar-H), 6.11 (1H, br s, NHCO), 5.72 (1H, br s, NHCO), 4.46 (2H, d, *J* 13.7, Ar–$\mathrm{CH_2}$–Ar *ax*), 4.45 (2H, d, *J* 13.7, Ar–$\mathrm{CH_2}$–Ar *ax*), 3.96 (4H, dt, *J* 7.2, *J* 6.0, 2 × $\mathrm{OCH_2}$), 3.76 (2H, t, *J* 7.2, $\mathrm{OCH_2}$), 3.73 (2H, t, *J* 7.7, $\mathrm{OCH_2}$), 3.16 (2H, d, *J* 13.2, Ar–$\mathrm{CH_2}$–Ar *eq*), 3.14 (2H, d, *J* 13.2, $\mathrm{CH_2}$-Ar *eq*), 1.97–1.88 (8H, m, 4 × $\mathrm{OCH_2C}\mathit{H}_2$), 1.07 (3H, t, *J* 7.7, $\mathrm{CH_3}$), 1.05 (3H, t, *J* 7.2, $\mathrm{CH_3}$), 0.93 (6H, t, *J* 7.2, 2 × $\mathrm{CH_3}$).

5,11-Bis(*N*′-phenylureido)-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) 3

To a stirred mixture of 100 mg (0.16 mmol) of 5,11-diamino-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) in 4 ml of dry dichloromethane 0.9 ml (7.2 mmol) of phenyl isocyanate was added. The mixture was stirred at room temperature for 12 h, poured into methanol, stirred for 30 min and evaporated to dryness. The residue was separated on 40 g of silica gel (petroleum ether–chloroform 2 : 1) and then by preparative TLC chromatography (petroleum ether–ethyl acetate 10 : 1) to yield 72 mg (52%) of **3** as a white powder, mp 171–174 °C (Found: C, 75.1; H, 7.0; N, 6.5. $\mathrm{C_{54}H_{60}N_4O_6}$ requires C 75.32; H 7.02; N 6.51%). δ_H (300 MHz; $\mathrm{CDCl_3}$–$\mathrm{(CD_3)_2SO}$ 10 : 1; $\mathrm{Me_4Si}$): 7.87 (2H, s, NHCO), 7.53 (2H, s, NHCO), 7.21 (4H, d, *J* 8.2, Ar-H), 7.04 (4H, t, *J* 7.7, Ar-H), 6.75 (2H, t, *J* 7.7, Ar-H), 6.64 (2H, s, Ar-H), 6.46–6.37 (6H, m, Ar-H), 6.31 (2H, s, Ar-H), 4.26 (1H, d, *J* 13.2, Ar–$\mathrm{CH_2}$–Ar *ax*), 4.21 (2H, d, *J* 12.6, Ar–$\mathrm{CH_2}$–Ar *ax*), 4.20 (1H, d, *J* 13.2, Ar–$\mathrm{CH_2}$–Ar *ax*), 3.65 (4H, t, *J* 7.7, 2 × $\mathrm{OCH_2}$), 3.59 (4H, t, *J* 7.6, 2 × $\mathrm{OCH_2}$), 2.95 (1H, d, *J* 13.2, Ar–$\mathrm{CH_2}$–Ar *eq*), 2.93 (2H, d, *J* 13.2, Ar–$\mathrm{CH_2}$–Ar *eq*), 2.86 (1H, d, *J* 13.2, Ar–$\mathrm{CH_2}$–Ar *eq*), 1.76–1.67 (8H, m, 4 × $\mathrm{OCH_2C}\mathit{H}_2$), 0.80 (12H, t, *J* 7.2, 4 × $\mathrm{CH_3}$).

5,11,17-Tris(*N*′-phenylureido)-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) 4

To a stirred mixture of 75 mg (0.11 mmol) of 5,11,17-triamino-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) in 4 ml of dry dichloromethane 0.38 ml (3.5 mmol) of phenyl isocyanate was added. The mixture was stirred at room temperature for 12 h, poured into methanol, stirred for 12 h and evaporated to dryness. The residue was separated on 40 g of silica gel (petroleum ether–chloroform 2 : 1) and then by preparative TLC chromatography (petroleum ether–ethyl acetate 10 : 1) to yield 65 mg (56%) of compound **4** as a yellowish powder, mp 208–210 °C (Found: C, 73.4; H, 6.6; N, 8.4. $\mathrm{C_{61}H_{66}N_6O_7}$ requires C 73.62; H 6.68; N 8.44%). δ_H (300 MHz; $\mathrm{CDCl_3}$–$\mathrm{(CD_3)_2SO}$ 10 : 1; $\mathrm{Me_4Si}$): 7.80 (1H, s, NHCO), 7.70 (2H, s, NHCO), 7.61 (1H, s, NHCO), 7.46 (2H, s, NHCO), 6.99 (2H, d, *J* 8.3, Ar-H), 6.89 (4H, d, *J* 7.7, Ar-H), 6.83–6.74 (6H, m, Ar-H), 6.54–6.46 (3H, m, Ar-H), 6.49 (2H, s, Ar-H), 6.42 (2H, d, *J* 7.7, Ar-H), 6.25 (1H, t, *J* 7.7, Ar-H), 6.23 (2H, s, Ar-H), 6.16 (2H, s, Ar-H), 4.02 (2H, d, *J* 12.7, Ar–$\mathrm{CH_2}$–Ar *ax*), 3.99 (2H, d, *J* 12.6, Ar–$\mathrm{CH_2}$–Ar *ax*), 3.54–3.44 (4H, m, 2 × $\mathrm{OCH_2}$), 3.31 (4H, t, *J* 7.2, 2 × $\mathrm{OCH_2}$), 2.72 (2H, d, *J* 13.6, Ar–$\mathrm{CH_2}$–Ar *eq*), 2.68 (2H, d, *J* 12.6, Ar–$\mathrm{CH_2}$–Ar *eq*), 1.60–1.45 (8H, m, 4 × $\mathrm{OCH_2C}\mathit{H}_2$), 0.61 (6H, t, *J* 7.2, 2 × $\mathrm{CH_3}$), 0.55 (6H, t, *J* 7.2, 2 × $\mathrm{CH_3}$).

5,17-Bis(*N*′-benzylureido)-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) 5

To a stirred mixture of 100 mg (0.16 mmol) of 5,17-diamino-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) in 4 ml of dry dichloromethane 0.2 ml (1.6 mmol) benzyl isocyanate was added. The mixture was stirred at room temperature for 60 h, poured into methanol, stirred for 24 h and evaporated to dryness. The residue was separated on 30 g of silica gel (petroleum ether–ethyl acetate 10 : 1) and then by preparative TLC chromatography (petroleum ether–ethyl acetate 4 : 1) to yield 62 mg (44%) of compound **5** as a yellowish powder, mp 151–154 °C (Found: C, 75.5; H, 7.2; N, 6.3. $\mathrm{C_{56}H_{64}N_4O_6}$ requires C 75.65; H 7.26; N 6.30%). δ_H (300 MHz; $\mathrm{CDCl_3}$; $\mathrm{Me_4Si}$): 7.32 (4H, m, Ar-H), 7.25 (4H, d, *J* 7.7, Ar-H), 7.12 (4H, d, *J* 7.7, Ar-H), 7.04 (2H, t, *J* 6.8, Ar-H), 6.93 (2H, t, *J* 7.2, Ar-H), 6.00 (4H, s, Ar-H), 4.46 (4H, d, *J* 13.4, Ar–$\mathrm{CH_2}$–Ar *ax*), 4.32 (4H, d , *J* 5.8, $\mathrm{NHC}\mathit{H}_2$-Ar), 4.01 (4H, t, *J* 8.3, 2 × $\mathrm{OCH_2}$), 3.67 (4H, t, *J* 6.6, 2 × $\mathrm{OCH_2}$), 3.16 (4H, d, *J* 14.3, Ar–$\mathrm{CH_2}$–Ar *eq*), 1.96–1.83 (8H, m, 4 × $\mathrm{OCH_2C}\mathit{H}_2$), 1.11 (6H, t, *J* 7.5, 2 × $\mathrm{CH_3}$), 0.87 (6H, t, *J* 7.5, 2 × $\mathrm{CH_3}$).

5,17-Bis(*N*′-cyclohexylureido)-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) 6

To a stirred mixture of 100 mg (0.16 mmol) of 5,17-diamino-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) in 4 ml of dry dichloromethane 0.4 ml (3.2 mmol) of cyclohexyl isocyanate was added. The mixture was stirred at room temperature for 60 h, poured into methanol, stirred for 30 min and evaporated to dryness. The residue was poured in 10 ml of acetone and filtered off to yield 72 mg (52%) of title compound **6** as a white precipitate, mp 192–195 °C (Found: C, 74.1; H, 8.2; N, 6.1. $\mathrm{C_{54}H_{72}N_4O_6}$ requires C 74.28; H 8.31; N 6.24). δ_H (300 MHz; $\mathrm{CDCl_3}$; $\mathrm{Me_4Si}$): δ: 7.29 (2H, s, NHCO), 7.04 (4H, d, *J* 7.7, Ar-H), 6.88 (2H, t, *J* 7.7, Ar-H), 5.86 (4H, s, Ar-H), 5.71 (2H, s, NHCO), 4.41 (4H, d, *J* 13.2, Ar–$\mathrm{CH_2}$–Ar *ax*), 3.95 (4H, t, *J* 8.2, 2 × $\mathrm{OCH_2}$), 3.66 (4H, t, *J* 6.6, 2 × $\mathrm{OCH_2}$), 3.62–3.44 (2H, m, H–Cy), 3.11 (4H, d, *J* 13.7, Ar–$\mathrm{CH_2}$–Ar *eq*), 1.92–1.81 (10H, m, 4 × $\mathrm{OCH_2C}\mathit{H}_2$ and H–Cy), 1.70–1.66 (4H, m, H–Cy), 1.62–1.58 (2H, m, H–Cy), 1.36–1.25 (6H, m, H–Cy), 1.28–1.08 (6H, m, H–Cy), 1.08 (6H, t, *J* 7.2, 2 × $\mathrm{CH_3}$), 0.86 (6H, t, *J* 7.2, 2 × $\mathrm{CH_3}$).

5,17-Bis(*N*′-phenylureido)-25,27-dipropoxycalix[4]arene-26,28-diol (*cone*) 7

To a stirred mixture of 100 mg (0.19 mmol) of 5,17-diamino-25,27-dipropoxycalix[4]arene-26,28-diol (*cone*) in 6 ml of dry dichloromethane 1.0 ml (9.3 mmol) of phenyl isocyanate was added to give a white precipitate. The mixture was stirred at room temperature for 12 h, poured into methanol and filtered off to yield 100 mg (70%) of compound **7** as a white powder, mp >350 °C (Found: C, 74.0; H, 6.1; N, 7.2. $C_{48}H_{48}N_4O_6$ requires C 74.21; H 6.23; N 7.21%). δ_H (300 MHz; $(CD_3)_2SO$, Me_4Si): 8.49 (2H, s, NHCO), 8.26 (2H, s, OH), 8.19 (2H, s, NHCO), 7.42 (4H, d, *J* 7.7, Ar-H), 7.25 (4H, t, *J* 8.0, Ar-H), 7.19 (4H, s, Ar-H), 7.04 (4H, d, *J* 7.2, Ar-H), 6.93 (2H, t, *J* 7.2, Ar-H), 6.81 (2H, t, *J* 7.5, Ar-H), 4.20 (4H, d, *J* 12.7, Ar–CH_2–Ar *ax*), 3.95 (4H, t, *J* 7.7, 2 × OCH_2), 3.41 (4H, d, *J* 13.2, Ar–CH_2–Ar *eq*), 2.01 (4H, m, 2 × $OCH_2C\mathit{H}_2$), 1.31 (6H, t, *J* 7.5, CH_3).

5,17-Bis[(*R*)-(−)-1-(1-naphthyl)ethylureido]-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) 8

To a stirred mixture of 100 mg (0.16 mmol) of 5,17-diamino-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) in 6 ml of dry dichloromethane 0.17 ml (0.96 mmol) (*R*)-(−)-1-(1-naphthyl)-ethyl isocyanate was added. The mixture was stirred at room temperature for 12 h, poured into methanol to give a white precipitate. The precipitate was filtered off to yield 96 mg (63%) of title compound **8** as a yellowish powder, mp 260–262 °C (Found: C, 77.8; H, 7.0; N, 5.5. $C_{66}H_{72}N_4O_6$ requires C 77.92; H 7.13; N 5.51%). δ_H (300 MHz; $CDCl_3$, Me_4Si): 8.05 (2H, m, Ar-H), 7.85 (2H, m, Ar-H), 7.76 (2H, m, Ar-H), 7.49–7.46 (4H, m, Ar-H), 7.39 (4H, s, Ar-H), 6.98 (2H, m, Ar-H), 6.92 (2H, m, Ar-H), 6.80 (2H, br s, NHCO), 6.56 (2H, br s, NHCO), 5.89 (4H, d, *J* 6.6, Ar-H), 5.73-5.66 (4H, m, CH and Ar-H), 4.38 (2H, d, *J* 13.2, Ar–CH_2–Ar *ax*), 4.36 (2H, d, *J* 13.7, Ar–CH_2–Ar *ax*), 3.93 (4H, t, *J* 7.7, 2 × OCH_2), 3.61 (4H, t, *J* 6.6, 2 × OCH_2), 3.08 (2H, d, *J* 14.2, Ar–CH_2–Ar *eq*), 3.02 (2H, d, *J* 14.8, Ar–CH_2–Ar *eq*), 1.92–1.81 (8H, m, 4 × $OCH_2C\mathit{H}_2$), 1.54 (6H, d, *J* 6.6, 4 × CH_3), 1.06 (6H, t, *J* 7.7, 2 × CH_3), 0.84 (6H, t, *J* 7.7, 2 × CH_3).

5,17-Bis(*N*′-phenylureido)-24,25,26,27-tetrapropoxycalix[4]arene (*partial cone*) 9

To a stirred mixture of 139 mg (0.22 mmol) of 5,17-diamino-24,25,26,27-tetrapropoxy-calix[4]arene (*partial cone*) in 4 ml of dry dichloromethane 0.6 ml (5.6 mmol) phenyl isocyanate was added to give a white precipitate. The mixture was stirred at room temperature for 12 h, poured into methanol, stirred for 30 min and evaporated to dryness. The residue was dissolved in chloroform and precipitated by methanol to yield 80 mg (42%) of **9** as a yellowish powder, mp 290–293 °C (Found: C, 75.1; H, 7.0; N, 6.5. $C_{54}H_{60}N_4O_6$ requires C 75.32; H 7.02; N 6.51). δ_H (300 MHz; $(CD_3)_2SO$, Me_4Si, 60 °C): 8.56 (1H, s, NHCO), 8.49 (1H, s, NHCO), 8.33 (1H, s, NHCO), 8.08 (1H, s, NHCO), 7.47 (4H, t, *J* 7,7, Ar-H), 7.35 (2H, s, Ar-H), 7.28 (2H, t, *J* 7.7, Ar-H), 7.27 (2H, t, *J* 7.7, Ar-H), 7.18 (2H, s, Ar-H), 6.96 (1H, t, *J* 7.7, Ar-H), 6.95 (1H, t, *J* 7.7, Ar-H), 6.88 (2H, d, *J* 7.2, Ar-H), 6.40 (2H, t, *J* 7.2, Ar-H), 6.32 (2H, d, *J* 7.7, Ar-H), 4.00 (2H, d, *J* 13.2, Ar–CH_2–Ar), 3.81–3.73 (2H, m, OCH_2), 3.65 (2H, t, *J* 7.2, OCH_2), 3.60 (2H, s, Ar–CH_2–Ar), 3.49 (2H, t, *J* 7.2, OCH_2), 3.28 (2H, s, Ar–CH_2–Ar), 3.00 (2H, d, *J* 13.2, Ar–CH_2–Ar), 1.92–1.77 (6H, m, 3 × $OCH_2C\mathit{H}_2$), 1.52–1.45 (2H, m, $OCH_2C\mathit{H}_2$), 1.06 (6H, t, *J* 7.7, 2 × CH_3), 0.99 (3H, t, *J* 7.7, CH_3), 0.68 (3H, t, *J* 7.7, CH_3) (one of the signals of OCH_2 is overlapped by signal of DMSO).

5,11,17,23-Tetrakis(*N*′-phenylureido)-24,25,26,27-tetrapropoxycalix[4]arene (1,3-*alternate*) 10

To stirred solution of 100 mg (0.15 mmol) of 5,11,17,23-tetraamino-24,25,26,27-tetrapropoxycalix[4]arene (1,3-*alternate*) in 6 ml of dry dichloromethane 0.83 ml (7.5 mmol) of phenyl isocyanate was added. The mixture was stirred at room temperature for 12 h and poured into methanol to give a clear solution. The mixture was stirred for 15 min and then evaporated to dryness. The residue was dissolved in small amount of methanol and stored overnight in a freezer to yield 86 mg (50%) of compound **10** as a yellowish powder, mp >350 °C (Found: C, 72.3; H, 6.3; N, 9.7. $C_{68}H_{72}N_8O_8$ requires C 72.32; H 6.43; N 9.92%; M^+ 1128,6). δ_H (300 MHz; $CDCl_3$, Me_4Si): 7.84 (4H, br s, NHCO), 7.73 (8H, d, *J* 8.2, Ar-H), 7.35 (8H, m, Ar-H), 7.09 (4H, t, *J* 7.2, Ar-H), 6.99 (8H, s, Ar-H), 6.56 (4H, br s, NHCO), 3.72 (8H, t, *J* 7.2, 4 × OCH_2), 3.47 (8H, s, Ar–CH_2–Ar), 1.88 (8H, m, 4 × $OCH_2C\mathit{H}_2$), 1.04 (12H, t, *J* 7.2, 4 × CH_3) $[M + Na]^+$ 1151.6.

5,11,17,23-Tetrakis(*N*′-benzylureido)-24,25,26,27-tetrapropoxycalix[4]arene (1,3-*alternate*) 11

To a stirred mixture of 100 mg (0.15 mmol) of 5,11,17,23-diamino-24,25,26,27-tetrapropoxycalix[4]arene (1,3-*alternate*) in 4 ml of dry dichloromethane 0.38 ml (3.0 mmol) benzyl isocyanate was added. The mixture was stirred at room temperature for 60 h, poured into methanol, stirred for 24 h and evaporated to dryness. The residue was dissolved in chloroform and precipitated by methanol to yield 42 mg (23%) of 5,11,17,23-tetrakis(*N*′-benzylureido)-24,25,26,27-tetrapropoxycalix[4]arene (1,3-*alternate*) **11** as a yellowish powder, mp 208–212 °C (Found: C, 72.7; H, 6.8; N, 9.4. $C_{72}H_{80}N_8O_8$ requires C 72.95; H 6.80; N 9.45%). δ_H (300 MHz; $CDCl_3$, Me_4Si): 7.34 (20H, br s, Ar-H), 6.89 (8H, s, Ar-H), 6.96–6.78 (4H, m, NHCO), 6.18–6.00 (4H, m, NHCO), 4.47 (8H, s, 4 × $NHC\mathit{H}_2$-Ar), 3.65 (8H, t, *J* 7.7, 4 × OCH_2), 3.38 (8H, s, Ar–CH_2–Ar), 1.92–1.82 (8H, m, 4 × $OCH_2C\mathit{H}_2$), 1.06 (12H, t, *J* 7.7, 4 × CH_3).

5,11,17,23-Tetrakis[(*R*)-(−)-1-(1-naphtyl)ethylureido]-24,25,26,27-tetrapropoxycalix[4]arene (1,3-*alternate*) 12

To a stirred mixture of 100 mg (0.15 mmol) of 5,11,17,23-tetraamino-24,25,26,27-tetrapropoxycalix[4]arene (1,3-*alternate*) in 6 ml of dry dichloromethane 0.32 ml (1.83 mmol) (*R*)-(–)-1-(1-naphtyl)ethyl isocyanate was added. The mixture was stirred at room temperature for 12 h, poured into methanol, stirred for 15 min and the white precipitate was filtered off to yield 160 mg (73%) of compound **12**, mp 307–308 °C (Found: C, 76.5; H, 6.7; N, 7.8. $C_{92}H_{96}N_8O_8$ requires C

76.64; H 6.71; N 7.77). δ_H (300 MHz; $CDCl_3$–CD_3OD 4 : 1, Me_4Si): 8.18 (4H, d, *J* 8.2, Ar-H), 7.87 (4H, d, *J* 8.8, Ar-H), 7.76 (4H, d, *J* 7.7, Ar-H), 7.55-7.42 (8H, m, Ar-H), 7.52 (8H, s, Ar-H), 6.93 (4H, s, Ar-H), 6.86 (4H, s, Ar-H), 5.78 (4H, q, *J* 6.6, CH), 3.55 (8H, t, *J* 7.2, 4 × OCH_2), 3.38 (8H, br s, Ar–CH_2–Ar), 1.76-1.68 (8H, m, 4 × OCH_2CH_2), 1.64 (12H, d, *J* 7.2, 4 × CH_3), 0.93 (12H, t, *J* 7.2, 4 × $CH_2CH_2CH_3$).

5,17-Bis(*N′*-phenylureido)-24,25,26,27-tetrapropoxycalix[4]arene (1,3-*alternate*) 13

To a stirred mixture of 70 mg (0.16 mmol) of 5,17-diamino-24,25,26,27-tetrapropoxycalix[4]arene (1,3-*alternate*) in 4 ml of dry dichloromethane 0.6 ml (5.6 mmol) of phenyl isocyanate was added. The mixture was stirred at room temperature for 12 h, poured into methanol, stirred for 30 min and evaporated to dryness. The residue was separated on 40 g of silica gel (petroleum ether–chloroform 2 : 1) and then by preparative TLC chromatography (petroleum ether–ethyl acetate 10 : 1) to yield 40 mg (42%) of compound **13** as a yellowish powder, mp 253–256 °C (Found C, 75.1; H, 7.0; N, 6.6. $C_{54}H_{60}N_4O_6$ requires C 75.32; H 7.02; N 6.51%). δ_H (300 MHz; $CDCl_3$, Me_4Si): 7.89 (2H, br s, NHCO), 7.73 (4H, d, *J* 8.2, Ar-H), 7.36–7.28 (4H, m, Ar-H), 7.09 (2H, t, *J* 7.2, Ar-H), 7.00 (4H, s, Ar-H), 6.98 (4H, d, *J* 7.7, Ar-H), 6.59 (2H, t, *J* 7.2, Ar-H), 6.52 (2H, br s, NHCO), 3.67 (4H, t, *J* 7.2, 2 × OCH_2), 3.66 (4H, t, *J* 7.2, 2 × OCH_2), 3.47 (8H, s, Ar–CH_2–Ar), 1.93-1.78 (8H, m, 4 × OCH_2CH_2), 1.10 (6H, t, *J* 7.7, 2 × CH_3), 0.95 (6H, t, *J* 7.2, 2 × CH_3).

5,17-Bis(*N*-benzoylamino)-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) 14

To a stirred solution of 100 mg (0.16 mmol) of 5,17-diamino-24,25,26,27-tetrapropoxycalix[4]arene (*cone*) in 2 ml of dry dichloromethane 0.05 ml (0.35 mmol) of triethyl amine and a solution of 0.04 ml (0.35 mmol) of benzoyl chloride in 2 ml of dry dichloromethane were added. The mixture was stirred at room temperature for 12 h, poured into 10 ml of 1 M HCl and extracted with 4 × 5 ml of chloroform. The organic layer was washed with 5 ml of brine and water and a 10% solution of potassium carbonate (to remove benzoic acid) and dried over magnesium sulfate to yield 51 mg (40%) of title compound **14** as a yellowish powder, mp 163–166 °C (Found: C, 77.9; H, 6.9; N, 3.4. $C_{54}H_{58}N_2O_6$ requires C 78.04; H 7.03; N 3.37%). δ_H (300 MHz; $CDCl_3$, Me_4Si): 7.62 (4H, m, Ar-H), 7.36 (2H, t, *J* 7.2, Ar-H), 7.22 (4H, d, *J* 7.7, Ar-H), 6.83 (4H, s, Ar-H), 6.76 (4H, d, *J* 7.2, Ar-H), 6.66 (2H, t, *J* 6.6, Ar-H), 4.47 (4H, d, *J* 13.2, Ar–CH_2–Ar *ax*), 3.90 (4H, t, *J* 7.7, 2 × OCH_2), 3.80 (4H, t, *J* 7.2, 2 × OCH_2), 3.16 (4H, d, *J* 13.2, Ar–CH_2–Ar *eq*), 1.97–1.88 (8H, m, 4 × OCH_2CH_2), 1.04–0.96 (12H, m, 4 × CH_3).

5,17-Dinitro-25,26,27,28-tetrapropoxycalix[4]arene (1,3-*alternate*) 15 and 5,17-dinitro-25,26,27,28-tetrapropoxycalix[4]arene (*partial cone*) 16

A mixture of 0.46 g (0.83 mmol) of 5,17-dinitro-25,27-dipropoxycalix[4]arene-26,28-diol, 2.5 g (7.5 mmol) of caesium carbonate and 0.8 ml (8.3 mmol) of propyl iodide were heated to 70 °C in 40 ml of dry *N*,*N*-dimethylformamide. The reaction was monitored by TLC chromatography (petroleum ether–chloroform 4 : 1). After 170 h the mixture was cooled, poured into 80 ml of 1 M HCl and extracted with 4 × 30 ml of chloroform. Combined extracts was washed by brine and water and dried over magnesium sulfate. After filtration the mixture was evaporated to dryness and separated on a column of 40 g silica gel (petroleum ether–chloroform 8 : 1). Finally, by preparative TLC chromatography (petroleum ether–chloroform 10 : 1) 136 mg (26%) of compound **15** (R_F = 0.4) and 350 mg (67%) of compound **16** (R_F = 0.9) were obtained as yellow powders. **15**: mp 229–232 °C (Found: C, 70.2; H, 6.5; N, 4.0. $C_{40}H_{46}N_2O_8$ requires C 70.36; H 6.79; N 4.10%). δ_H (300 MHz; $CDCl_3$, Me_4Si): 7.94 (4H, s, Ar-H), 7.01 (4H, d, *J* 7.7, Ar-H), 6.72 (2H, t, *J* 7.7, Ar-H), 3.69 (4H, t, *J* 7.7 Hz, 2 × OCH_2), 3.64 (8H, s, Ar–CH_2–Ar), 3.62 (4H, t, *J* 7.7, 2 × OCH_2), 1.84–1.69 (8H, m, 4 × OCH_2CH_2), 1.00 (6H, t, *J* 7.2, 2 × CH_3), 0.96 (6H, t, *J* 7.2, 2 × CH_3). **16**: mp 212–215 °C (Found: C, 70.1; H, 6.7; N, 4.0. $C_{40}H_{46}N_2O_8$ requires C 70.36; H 6.79; N 4.10%). δ_H (300 MHz; $CDCl_3$, Me_4Si): 8.22 (2H, s, Ar-H), 8.03 (2H, s, Ar-H), 6.94 (2H, d, *J* 7.1, Ar-H), 6.48 (2H, t, *J* 7.7, Ar-H), 6.27 (2H, d, *J* 7.3, Ar-H), 4.09 (2H, d, *J* 13.2, Ar–CH_2–Ar), 3.88 (2H, t, *J* 7.7, OCH_2), 3.84–3.78 (2H, m, OCH_2), 3.79–3.67 (4H, m, Ar–CH_2–Ar), 3.61–3.53 (2H, m, OCH_2), 3.39–3.34 (2H, m, OCH_2), 3.18 (2H, d, *J* 13.7, Ar–CH_2–Ar), 1.43–1.31 (2H, m, OCH_2CH_2), 2.00–1.91 (6H, m, 3 × OCH_2CH_2), 1.13 (6H, t, *J* 7.2, 2 × CH_3), 1.11 (3H, t, *J* 7.2, CH_3), 0.65 (3H, t, *J* 7.7, CH_3).

Preparation of appropriate amino derivatives—general procedure

The procedure is adapted according to published procedures:[8,9] 0.5 mmol of nitro derivative was mixed with *n* × 2.5 mmol of $SnCl_2 \cdot 2H_2O$ (*n* × 0.56 g, where *n* is the number of nitro groups in the molecule of the starting calix[4]arene) and dissolved in 30 ml of ethanol. The mixture was refluxed for 12 h, the solvent was then evaporated and the residue was dissolved in a mixture of 30 ml of chloroform and 30 ml of 1 M KOH. The organic layer was separated, and the aqueous layer was extracted with 3 × 20 ml of chloroform. The extracts was combined, dried over magnesium sulfate and evaporated to dryness. The following amines were obtained.

5,11,17-Triamino-25,26,27,28-tetrapropoxycalix[4]arene (*cone*) 17

Yield: 214 mg (67%), dark yellow powder (Found: C, 75.2; H, 8.0; N, 6.5. $C_{40}H_{51}N_3O_4$ requires C 75.32; H 8.06; N 6.59%). δ_H (300 MHz; $CDCl_3$, Me_4Si): 6.72 (2H, d, *J* 6.6, Ar-H), 6.65 (1H, t, *J* 6.6, Ar-H), 6.08 (2H, s, Ar-H), 6.00 (2H, s, Ar-H), 5.96 (2H, s, Ar-H), 4.40 (2H, d, *J* 13.7, Ar–CH_2–Ar *ax*), 4.32 (2H, d, *J* 13.2, Ar–CH_2–Ar *ax*), 3.85 (2H, t, *J* 7.2, 1 × OCH_2), 3.73 (6H, t, *J* 7.2, 3 × OCH_2), 3.64 (2H, m, NH_2), 3.18 (4H, br s, NH_2), 3.05 (2H, d, *J* 13.2, Ar–CH_2–Ar *eq*), 2.92 (2H, d, *J* 13.2, Ar–CH_2–Ar *eq*), 1.91–1.84 (8H, m, 4 × OCH_2CH_2), 1.01–0.93 (12H, br t, *J* 7.7, 4 × CH_3).

5,17-Diamino-25,26,27,28-tetrapropoxycalix[4]arene (1,3-*alternate*) 18

Yield: 57 mg (from 0,1 mmol of nitro derivative, 92%), dark yellow powder (Found: C, 77.0; H, 8.0; N, 4.4. $C_{40}H_{50}N_2O_4$

requires C 77.14; H 8.09; N 4.50%). δ_H (300 MHz; $CDCl_3$, Me_4Si): 6.98 (4H, d, J 7.7, Ar-H), 6.63 (2H, t, J 7.2, Ar-H), 6.47 (4H, s, Ar-H), 3.52 (8H, s, Ar–CH_2–Ar), 3.50 (8H, m, 4 × OCH_2), 3.14 (4H, m, NH_2), 1.78–1.62 (8H, m, 4 × OCH_2C-H_2), 1.01 (6H, t, J 7.7, 2 × CH_3), 0.95 (6H, t, J 7.7, 2 × CH_3).

5,17-Diamino-25,26,27,28-tetrapropoxycalix[4]arene (*partial cone*) 19

Yield: 215 mg (69%), dark yellow powder (Found: C, 77.0; H, 8.0; N, 4.4. $C_{40}H_{50}N_2O_4$ requires C 77.14; H 8.09; N 4.50%). δ_H (300 MHz; $CDCl_3$, Me_4Si): 6.92 (2H, d, J 7.2, Ar-H), 6.57 (2H, s, Ar-H), 6.48 (2H, s, Ar-H), 6.43 (2H, t, J 7.7, Ar-H), 6.36 (2H, d, J 7.7, Ar-H), 4.02 (2H, d, J 13.2, Ar–CH_2–Ar), 3.77–3.68 (2H, m, OCH_2), 3.69 (2H, t, J 7.7, OCH_2), 3.55 (2H, s, Ar–CH_2–Ar), 3.53 (2H, s, Ar–CH_2–Ar), 3.51 (2H, t, J 7.7, OCH_2), 3.38 (4H, br s, NH_2), 3.33–3.27 (2H, m, OCH_2), 2.92 (2H, d, J 13.2, Ar–CH_2–Ar), 1.93–1.82 (4H, m, 2 × OCH_2C-H_2), 1.59–1.51 (4H, m, 2 × OCH_2CH_2), 1.09 (6H, t, J 7.7, 2 × CH_3), 1.04 (3H, t, J 7.2, CH_3), 0.78 (3H, t, J 7.2, CH_3).

Crystallography. $C_{54}H_{60}N_4O_6 \cdot C_2H_5OH \cdot H_2O$ **19**, M = 931.23 g mol^{-1}, orthorhombic system, space group $P2_12_12_1$, a = 15.2889(2), b = 17.4579(3), c = 18.7828(4) Å, Z = 4, V = 5013.36(10) $Å^3$, D_c = 1.14 g cm^{-3}, μ(Mo-Kα) = 0.074 mm^{-1}, crystal dimensions of 0.3 × 0.5 × 0.3 mm. Data were collected at 150(2) K on a Nonius KappaCCD diffractometer with graphite monochromated Mo-Kα radiation. The structure was solved by direct methods[18] using the CRYSTALS suite of programs[19] and anisotropically refined by full-matrix least squares on F values to final R = 0.0397 and Rw = 0.0474 using 6300 independent reflections (θ_{max} = 27.47°) and 649 parameters. The positions of disordered groups were found from the electron density maps. Disordered fragments were then placed in appropriate positions, and all distances between neighbouring atoms and angles were fixed. Site occupancies were refined for the different parts with the same thermal parameters for the same atoms in the various fragments. At the end of refinement, site occupancies were fixed and hydrogen atoms were placed in calculated positions.

CCDC reference number 678255. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b802871k

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References

1 (*a*) J. L. Sessler, P. A. Gale and W.-S. Cho, *Anion Receptor Chemistry*, The Royal Society of Chemistry, Cambridge, 2006; (*b*) P. Lhoták, *Top. Curr. Chem.*, 2005, **255**, 65–96; (*c*) P. A. Gale, *Coord. Chem. Rev.*, 2001, **213**, 79; (*d*) P. A. Gale, *Coord. Chem. Rev.*, 2000, **199**, 181; (*e*) P. D. Beer and E. J. Hayes, *Coord. Chem. Rev.*, 2003, **240**, 167; (*f*) M. D. Best, S. L. Tobey and E. V. Anslyn, *Coord. Chem. Rev.*, 2003, **240**, 3; (*g*) C. Suksai and T. Tuntulani, *Chem. Soc. Rev.*, 2003, 192; (*h*) R. J. Fitzmaurice, G. M. Kyne, D. Dougheret and J. D. Kilburn, *J. Chem. Soc., Perkin Trans. 1*, 2002, 841; (*i*) P. A. Gale and P. D. Beer, *Angew. Chem., Int. Ed.*, 2001, **40**, 487; (*j*) *Supramolecular Chemistry of Anions*, ed. A. Bianchi, K. Bowman-James and E. Garcia-Espana, Wiley-VCH, New York, 1997; (*k*) F. P. Schmidtchen and M. Berger, *Chem. Rev.*, 1997, **97**, 1609.

2 (*a*) B. J. Hay, T. K. Firman and B. A. Moyer, *J. Am. Chem. Soc.*, 2005, **127**, 1810; (*b*) C. R. Bondy and S. J. Loeb, *Coord. Chem. Rev.*, 2003, **240**, 77; (*c*) K. Choi and A. D. Hamilton, *Coord. Chem. Rev.*, 2003, **240**, 101; (*d*) P. D. Beer, A. G. Cheetham, M. G. B. Drew, O. D. Fox, E. J. Hayes and T. D. Rolls, *Dalton Trans.*, 2003, 603.

3 For books on calixarenes see: (*a*) *Calixarenes 2001*, ed. Z. Asfari, V. Böhmer, J. Harrowfield and J. Vicens, Kluwer Academic Publishers, Dordrecht, 2001; (*b*) L. Mandolini and R. Ungaro, *Calixarenes in Action*, Imperial College Press, London, 2000; (*c*) C. D. Gutsche, *Calixarenes Revisited*, Monographs in Supramolecular Chemistry, ed. J. F. Stoddart, The Royal Society of Chemistry, Cambridge, 1998, vol. 6; (*d*) *Calixarenes 50th Anniversary: Commemorative Issue*, ed. J. Vicens, Z. Asfari and J. M. Harrowfield, Kluwer Academic Publishers, Dordrecht, 1994; (*e*) *Calixarenes: A Versatile Class of Macrocyclic Compounds*, ed. J. Vicens and V. Böhmer, Kluwer Academic Publishers, Dordrecht, 1991.

4 (*a*) A. Casnati, F. Sansone and R. Ungaro, Calixarene Receptors in Ion Recognition and Sensing, in *Advances in Supramolecular Chemistry*, ed. G. W. Gokel, Cerberus Press Inc., South Miami, 2004, pp. 169–218, vol. 9; (*b*) P. Lhoták, Anion Receptors Based on Calixarenes, *Top. Curr. Chem.*, 2005, **255**, 65–96, and references therein; (*c*) A. V. Yakovenko, V. I. Boyko, V. I. Kalchenko, L. Baldini, A. Casnati, F. Sansone and R. Ungaro, *J. Org. Chem.*, 2007, **72**, 3223; (*d*) B. Schazmann and D. Diamond, *New J. Chem.*, 2007, **31**, 587–592.

5 (*a*) P. A. Gale, *Coord. Chem. Rev.*, 2003, **240**, 191; (*b*) M. M. G. Antonisse and D. N. Reinhoudt, *Chem. Commun.*, 1998, 443.

6 (*a*) I. Stibor, S. M. H. Dana, P. Lhoták, J. Hodačová, J. Koča and M. Čajan, *Gazz. Chim. Ital.*, 1997, **127**, 673; (*b*) M. Čajan, I. Stibor and J. Koča, *J. Phys. Chem. A*, 1999, **103**, 3778; (*c*) M. Čajan, J. Damborský, I. Stibor and J. Koča, *J. Chem. Inf. Comput. Sci.*, 2000, **40**, 1151; (*d*) I. Stibor, R. Holakovský, A. M. Mustafina and P. Lhoták, *Collect. Czech. Chem. Commun.*, 2004, **69**, 365; (*e*) J. Budka, P. Lhoták, V. Michlová and I. Stibor, *Tetrahedron Lett.*, 2001, **42**, 1583; (*f*) V. Šťastná, P. Lhoták, V. Michlová, I. Stibor and J. Sykora, *Tetrahedron*, 2002, **58**, 7207; (*g*) M. Dudič, P. Lhoták, I. Stibor, K. Lang and P. Prošková, *Org. Lett.*, 2003, **5**, 149; (*h*) P. Lhoták, J. Svoboda, Jr and I. Stibor, *Tetrahedron*, 2006, **62**, 1253.

7 (*a*) W. Verboom, S. Datta, Z. Asfari, S. Harkema and D. N. Reinhoudt, *J. Org. Chem.*, 1992, **57**, 5394; (*b*) A. Casnati, F. Bonetti, F. Sansone, F. Ugozzoli and R. Ungaro, *Collect. Czech. Chem. Commun.*, 2004, **69**, 1063.

8 G. Mislin, E. Graf and M. W. Hosseini, *Tetrahedron Lett.*, 1996, **37**, 4503.

9 A. M. A. van Wageningen, E. Snip, W. Verboom, D. N. Reinhoudt and H. Boerrigter, *Liebigs Ann.*, 1997, 2235.

10 P. Timmerman, H. Boerrigter, W. Verboom and D. N. Reinhoudt, *Recl. Trav. Chim. Pays-Bas*, 1995, **114**, 103.

11 O. Struck, L. A. J. Chrisstoffels, R. J. W. Lugtenberg, W. Verboom, G. J. van Hummel, S. Harkema and D. N. Reinhoudt, *J. Org. Chem.*, 1997, **62**, 2487.

12 S. E. Matthews, M. Saadioui, V. Böhmer, S. Barboso, F. Arnaud-Neu, M.-J. Schwing-Weill, A. G. Carrera and J.-F. Dozol, *J. Prakt. Chem./Chem.-Ztg.*, 1999, **341**, 264.

13 R. K. Castellano and J. Rebek, Jr, *J. Am. Chem. Soc.*, 1998, **120**, 3657.

14 The stoichiometry of complexes and the complexation constants were calculated using the computer program OPIUM (M. Kyvala) freely available at http://www.natur.cuni.cz/~kyvala/opium.html.

15 For leading references of aromatic stacking interactions, see: (*a*) C. A. Hunter, K. R. Lawson, J. Perkins and C. J. Urch, *J. Chem. Soc., Perkin Trans. 2*, 2001, 651; (*b*) S. L. Cockkroft, J. Perkins, C. Zontaq, H. Adams, S. E. Spey, C. M. R. Low, J. G. Winter, K. R. Lawson, C. J. Urch and C. A. Hunter, *Org. Biomol. Chem.*, 2007, **5**, 1062; for interaction of halide anions with electron deficient arenas, see: O. B. Berryman, V. S.

Bryantsev, D. P. Stay, D. W. Johnson and B. P. Hay, *J. Am. Chem. Soc.*, 2007, **129**, 48.

16 For examples see: (*a*) O. Mogck, V. Böhmer and W. Vogt, *Tetrahedron*, 1996, **52**, 8489; (*b*) O. Mogck, E. F. Paulus, V. Böhmer, I. Thondorf and W. Vogt, *Chem. Commun.*, 1996, 2533; (*c*) O. Mogck, M. Pons, V. Böhmer and W. Vogt, *J. Am. Chem. Soc.*, 1997, **119**, 5706; (*d*) M. M. Conn and J. Rebek, Jr, *Chem. Rev.*, 1997, **97**, 1647; (*e*) J. Rebek, Jr, *Chem. Commun.*, 2000, 637; (*f*) J. de Mendoza, *Chem. Eur. J.*, 1998, **4**, 1373; (*g*) M. S. Brody, C. A. Schalley, D. M. Rudkevich and J. Rebek, Jr, *Angew. Chem., Int. Ed.*, 1999, **38**, 1640; (*h*) Y. L. Cho, D. M. Rudkevich, A. Shivanyuk, K. Rissanen and J. Rebek, Jr, *Chem. Eur. J.*, 2000, **6**, 3788; (*i*) Y. L. Cho, D. M. Rudkevich and J. Rebek, Jr, *J. Am. Chem. Soc.*, 2000, **122**, 9868.

17 K. Lang, P. Cuřínová, M. Dudič, P. Prošková, I. Stibor, V. Šťastný and P. Lhoták, *Tetrahedron Lett.*, 2005, **46**, 4469.

18 A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori and R. Spagna, *J. Appl. Crystallogr.*, 1999, **32**, 115.

19 P. W. Betteridge, J. R. Carruthers, R. I. Cooper, K. Prout and D. J. Watkin, *J. Appl. Crystallogr.*, 2003, **36**, 1487.