Anion recognition by diureido-calix[4]arenes in the 1,3-*alternate* conformation†

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A series of diureido-calix[4]arenes immobilised in the *1,3-alternate* conformation was synthesised and systematically studied for their complexation ability. As revealed by ^{1}H NMR and UV/vis titrations, this structural motif leads to very efficient ligands for anion recognition with high binding constants in nonpolar solvents. The comparison with the corresponding ligands possessing the *cone* conformation indicates that diureido-calix[4]arene in a *1,3-alternate* conformation are very promising anion receptors with pronounced binding ability towards carboxylates.

Introduction

The importance of anions in biological systems, chemical processes, or environmental pollution is well recognised. For this reason, the anion recognition plays an important role in supramolecular chemistry as can be documented by numerous reviews published recently.[1] In the design of novel anion-complexing ligands the three main strategies have been developed: (i) ligands using electrostatic interactions with anions (cationic, polyammonium, quanidinium, quaternary ammonium, porphyrin-based ligands); (ii) neutral ligands based on the variety of Lewis-acids (derivatives bearing tin, silicon, boron, mercury, uranyl, or other metal moieties); and (iii) neutral ligands allowing hydrogen bonding interactions. Not surprisingly, considerable effort has been devoted to the design of the last group of receptors, as neutral organic ligands with hydrogen bonding functionalities possess some remarkable advantages.[2] Neutral receptors are usually pH insensitive and there is generally no competition with a counter anion as contrast to the protonated anion receptors from the group (i). Furthermore, it is known that anionic species have a wide range of geometries depending on the nature of anion. Correspondingly, the design of anionic receptors is especially challenging when compared with those for cations because the successful binding of anions requires higher degree of preorganisation, interaction directionality, and complementarity. Neutral ligands can thus benefit from the anisotropy of hydrogen bonding and can be used for the construction of highly preorganised and selective anion receptors.

Calix[4]arenes are frequently used in the role of molecular scaffolds, as they are versatile macrocyclic compounds with tuneable 3D-shapes of their skeleton, well established chemistry, and abundant literature resources.[3] Many neutral calixarene-based ligands designed for binding of anions[4] or cation–anion couples[5] have been described so far. Our own research has been oriented to anion recognition using simple (hetero)aromatic amides,[6a–c] ureas,[6d] or calixarene-based ligands.[6e–i] Recently, we have described a series of new bis- to tetrakis-(ureido)calix[4]arenes in the *cone* conformation[6j] and we have demonstrated that these compounds can be extremely efficient ligands for complexation of anions possessing different binding geometries. Here we report on the synthesis and complexation ability of ureido-calix[4]arenes having two arylurea units appended to the upper rim of the calix[4]arene skeleton. Immobilisation in the *1,3-alternate* conformation can make these derivatives even more efficient when compared with the corresponding *cone* analogues as documented by extremely high binding constants in nonpolar solvents.

Results and discussion

Design

The systematic study of neutral ligands based on ureido-calixarenes for anion recognition revealed that tetrapropoxy-calix[4]arene bearing two ureido moieties on the upper rim is the versatile structural motif with an excellent ability to bind anions.[6j] To our surprise, ligand **2** in the *1,3-alternate* conformation showed better affinity towards anions than corresponding *cone* derivative **1** indicating that the *1,3-alternates* represent a promising conformation in the design of novel anion receptors. Based on this finding we have designed a series of six receptors **7–12** in the *1,3-alternate* conformation (Fig. 1). As we have encountered some problems with a low solubility of derivative **2**,[6j] we introduced two hexyl groups to enhance the solubility in common organic solvents. The propyl groups on the "ureido-side" of the scaffold are

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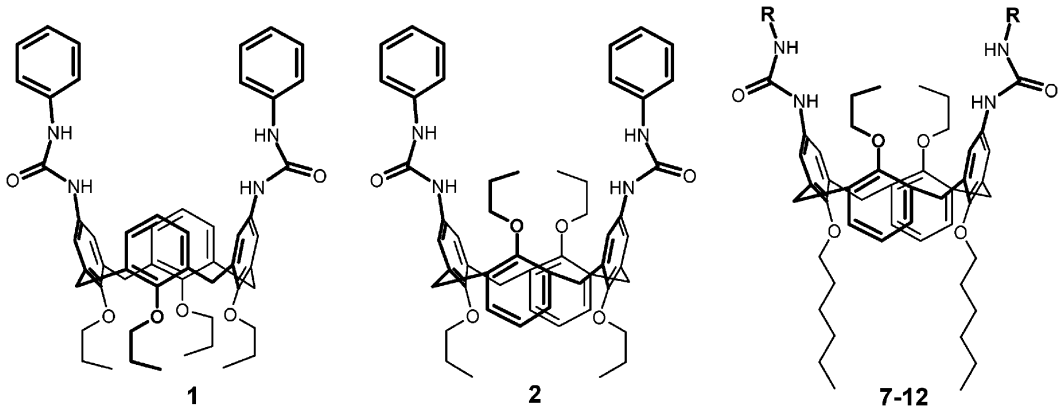

Fig. 1 Prepared urea derivatives of calix[4]arene.

necessary for the "freezing" of the conformation and our previous results did not show steric hindrance effects for the binding of anions. The group **R** in formulae **7–12** stands for different substituents used to evaluate the structure-complexation ability relationship. Thus, phenyl (**7**), benzyl (**8**), phenylsulfonyl (**9**), benzoyl (**10**), chloroacetyl (**11**) and *p*-nitrophenyl (**12**) groups were used.

Synthesis

The compounds **7–12** were prepared using a similar procedure as reported for compound **2**.[6j] In general, the whole synthetic pathway can be described by the sequence: (i) alkylation of starting calix[4]arene to 25,27-dipropoxycalix[4]arene,[7a,b] (ii) nitration to 5,17-dinitro-25,27-dipropoxycalix[4]arene,[7c,d] (iii) subsequent alkylation with hexyl iodide to 5,17-dinitro-26,28-dihexyloxy-25,27-dipropoxycalix[4]arene, (iv) reduction to 5,17-diamino-derivative, (v) reaction with aryl isocyanate to form appropriate bis(ureido)-calix [4]arenes **7–12** (Fig. 2).

Nitration of dipropoxycalix[4]arene using a well established procedure[8] led regioselectively to the corresponding dinitro derivative **3** with *p*-nitrated free phenolic rings. Subsequent alkylation to corresponding *1,3-alternate* **4** is a key step, and at the same time the bottle-neck of the whole reaction sequence. The best yield was achieved using similar reaction conditions as applied for the preparation of derivative **2**.[6j] Alkylation of dipropoxy derivative **3** with hexyl iodide in DMF using caesium carbonate as a base led to a mixture of two conformers **4** and **5** in 17 and 70% yields, respectively. Unfortunately, despite our substantial effort, the variations in the base, solvent, and reaction temperature did not improve yields of the *1,3-alternate* **4**, and the unwished *partial cone* conformation **5** was always the main product. The separation of these two conformers can be achieved only by column chromatography which makes the synthesis of pure **4** somewhat laborious despite the great difference in the chromatographic mobility of both isomers (R_F[4] = 0.3 and R_F[5] = 0.9). The pure *1,3-alternate* isomer **4** was then reduced by $SnCl_2$ dihydrate in ethanol[7d,9,10] to give the corresponding *1,3-alternate* derivative **6** in 89% yield. The synthesis of **7–12** was finally achieved in 40–60% yields using a standard reaction protocol[11] with commercially available isocyanates.

Complexation

The complexation behaviour of novel ligands was investigated by standard ^{1}H NMR titration experiments using a constant calixarene concentration (0.1–2.0 mM) and an increasing concentration of appropriate anion to obtain different host : guest ratios (0.1–20 : 1).[6e] To ensure the solubility of both organic (ligands) and inorganic (anions) constituents, a mixed solvent system ($CDCl_3$–CD_3CN = 4 : 1, v/v) was used. All anions were added as their tetrabutylammonium salts to minimise possible interactions of calixarenes with counter cations. The addition of anions led to the down-field shifts of –NH– signals in the ^{1}H NMR spectra indicating the complexation phenomenon under fast exchange conditions. Unfortunately, the signals of –NH– protons became broadened (and sometimes even completely disappeared), hence, the binding constants were determined from the complexation induced shifts (CIS) of neighbouring aromatic CH protons (*meta*-positions). These shifts were usually 20–50 Hz upon the addition of 2.5 equivalents of anions. Fig. 3 shows a typical binding isotherm indicating the formation of a 1 : 1 complex. The stoichiometry of the complexation was also confirmed by the corresponding Job plots. The results obtained are summarised in Table 1 where previously described compound **1** has been taken as a reference.[6j] The binding constants of novel receptors **7**, **9** and **12** towards some anions were too large to be measured accurately by ^{1}H NMR spectroscopy and the values given are rough estimations.

As follows from Table 1, the *1,3-alternate* calix[4]arene-based ureas are very effective receptors for anions in organic solvent, especially, when the structural motif based on aromate-urea-aromate is constructed. A direct comparison of otherwise identical ligands **1** and **7** (possessing different conformations) indicates that the *1,3-alternate* conformation (compound **7**) leads to much higher complexation constants if compared with the *cone* receptor **1**. This phenomenon can be ascribed to the higher rigidity of a *1,3-alternate* conformation compared with the *cone* analogue. It is known that in the case of the *cone* conformers so-called *pinched cone–pinched cone* equilibrium[12] occurs in solution, and these additional conformational movements should be generally unfavourable for

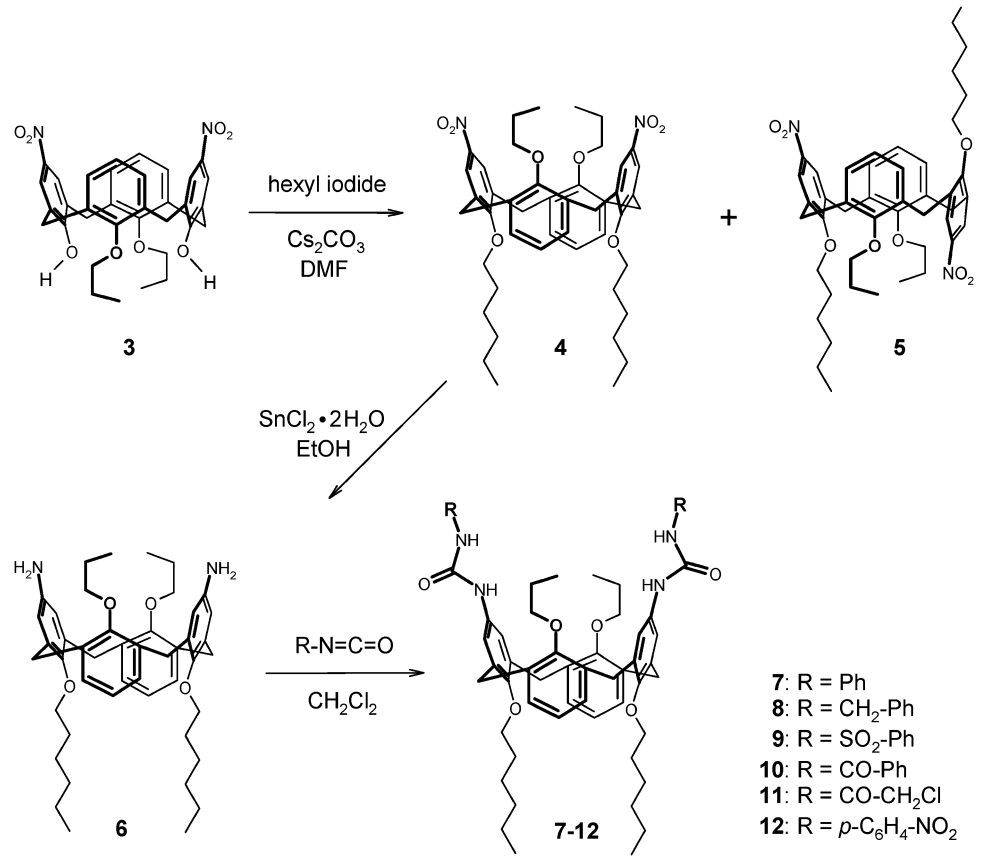

Fig. 2 Synthetic pathway to anion receptors **7–12**.

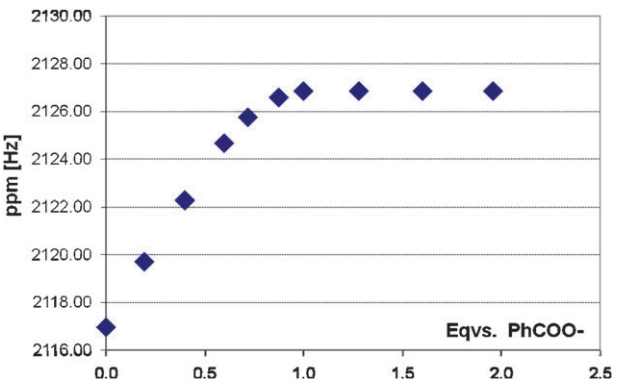

Fig. 3 Binding isotherm of ligand **7** with BzO^- anion.

the complexation phenomenon. On the other hand, no similar additional mobility was observed in the *1,3-alternate* derivatives.

The insertion of one –CH_2– group between the urea moiety and the aromatic calix[4]arene core in **8** causes a dramatic decrease in the complexation ability (compare $K_{Cl} = 5 \times 10^4$ M^{-1}, $K_{Br} = 8 \times 10^3$ M^{-1} for **7** *vs.* $K_{Cl} = 1300$ M^{-1}, $K_{Br} = 930$ M^{-1} for **8**). When the aromatic ring is connected to the urea moiety *via* the electron-withdrawing sulfonyl group (ligand **9**), the complexation abilities towards anions increased.

On the other hand, compound **10** with the electron-withdrawing carbonyl group as a spacer showed only negligible changes in the ^{1}H NMR spectra upon the addition of anions. This unexpected difference in the behaviour of structurally related compounds **9** and **10** can be explained by the analysis of the crystallographic results. It was revealed that compound **10** forms very strong *intramolecular* hydrogen bonds between –NH– and –CO– groups in the solid state as shown in Fig. 4. The H···O distances are 1.87 and 1.91 Å. The similar hydrogen bonding pattern was found in the crystal

Table 1 Binding constants of ligands **7–12** towards selected anions (^{1}H NMR titration, 300 MHz, $CDCl_3$–CD_3CN = 4 : 1, v/v, 25 °C)

	K/M^{-1}						
Anion	**1**[6j]	**7**	**8**	**9**	**10**	**11**	**12**
Chloride	4700 ± 490	50 000 ± 9000	1300 ± 160	10^5	[a]	110 ± 10	$>10^6$
Bromide	1400 ± 160	8000 ± 1200	930 ± 200	3500 ± 450	—	80 ± 20	—
Acetate	4000 ± 1100	35 000 ± 6000	5700 ± 180	10^5	[a]	3900 ± 200	80 000 ± 10 000
Benzoate	(1.6 ± 0.45) × 10^5	$>10^6$	6000 ± 1100	$>10^6$	1700 ± 200	800 ± 100	$>10^6$

[a] No visible changes (CIS <5 Hz).

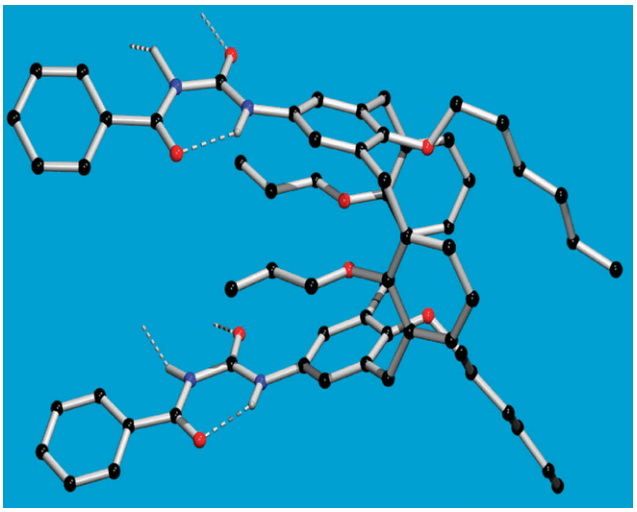

Fig. 4 Intramolecular hydrogen bonding pattern in the crystal structure of ligand **10** (other hydrogen atoms are omitted for better clarity).

structures of simple acylureido derivatives.[13] The intramolecular hydrogen bonding is highly probable even in solution as documented by the comparison of ^{1}H NMR spectra. The signals of –NH– protons in **7** are at 7.91 and 6.46 ppm, while the same signals in **10** can be found at 10.92 and 10.49 ppm. The pronounced low-field shift in compound **10** indicates strong intramolecular hydrogen bonding that might be responsible for the negligible complexation ability of ligand **10**. Furthermore, compound **10** forms an interesting dimeric motif in the solid state where two molecules are interconnected *via* four *intermolecular* hydrogen bonds (Fig. 5).

In ligand **11**, the aliphatic chain is attached to the urea moiety. Although the complexation ability of this receptor is generally reduced compared to its aromatic analogue **7**, an exceptional selectivity towards acetate was observed.

As the *p*-nitrophenyl group is a chromophore, the complexation properties of **12** were complemented using UV/Vis titration experiments (Table 2, Fig. 6).[17] The increasing amount of anions led to a red shift of the *p*-nitrophenyl absorption band and the obtained set of recorded absorption

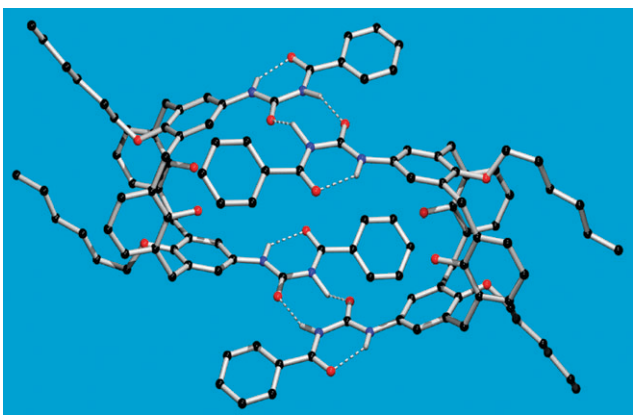

Fig. 5 Dimeric motif in the crystal packing of ligand **10** connected *via* intermolecular hydrogen bonds (other hydrogen atoms and propyl groups are omitted for better clarity).

Table 2 Binding constants K/M^{-1} of receptor **12** with selected anions (UV/Vis titration, CH_2Cl_2, 298 K)

Anion[a]	K/M^{-1}
Cl^-	$2.8 \times 10^{7\,b}$
Br^-	$>10^6$
I^-	1.9×10^5
NO_3^-	3.9×10^5
BzO^-	$5 \times 10^{7\,b}$

[a] Anions were added as tetrabutylammonium salts. Estimated error is 15%. [b] A larger standard deviation (35%) is due to almost linear titration curves causing ill-effects during the least-squares fitting procedure.

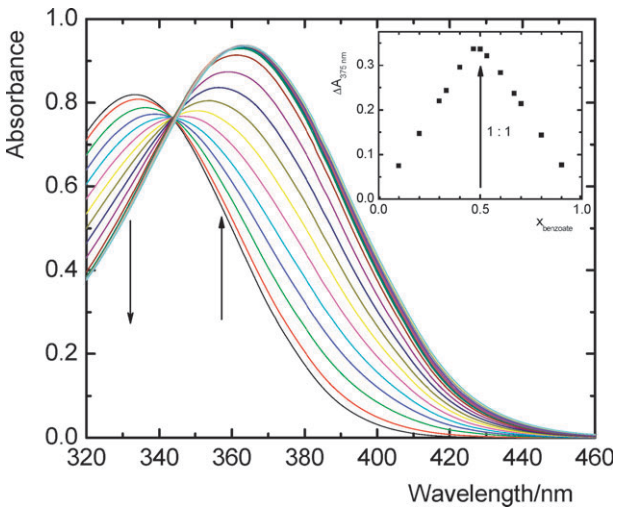

Fig. 6 UV/Vis titration of **12** (2.7×10^{-5} M) with benzoate in CH_2Cl_2; arrows show changes due to increasing concentration of benzoate up to 2.1×10^{-3} M. Inset: the corresponding Job plot documenting the 1 : 1 stoichiometry of the complex. The plot was constructed from absorbance changes at 375 nm using the sum of concentrations 3.2×10^{-5} M.

spectra was globally analyzed to obtain the corresponding binding constants. The interaction between –NH and anions is much stronger when compared to the structurally equivalent calix[4]arenes **1** and **7** (Tables 1 and 2) since the nitro group makes the benzene ring electron deficient thus increasing the hydrogen bond donating capability of the N–H groups. Our results also demonstrate that **12** is an effective binder even for non-spherical anions such as NO_3^- and BzO^-.

Compound **12** binds strongly Cl^-, Br^- and BzO^- so that the binding isotherms exhibit a sharp saturation beyond the molar concentration ratio of 1 : 1 indicating the stoichiometry 1 : 1 and the binding constants above 10^6 M^{-1}. The stoichiometry of complexes was confirmed by Job plot analysis. Thus, the binding isotherms, the observed isosbestic points, and corresponding Job plots clearly indicate that a 1 : 1 complex is formed between **12** and anions (Fig. 6). The binding site is created by two diametrically placed ureas that offer four hydrogen-bonding interactions for the binding of anions in between. The importance of multipoint interactions on the efficiency of the binding follows clearly from the comparison of **12** with model calixarene bearing only one nitrophenyl-urea

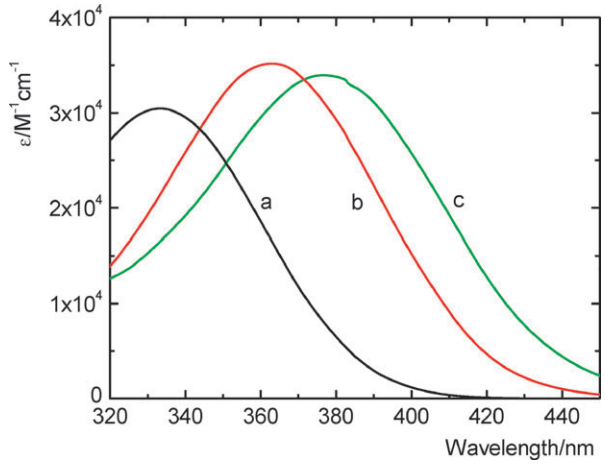

Fig. 7 Absorption spectra of **12** (a), **12**-BzO^- (b) and **12**-$(BzO^-)_2$ (c) in CH_2Cl_2. The absorption spectrum of **12**-$(BzO^-)_2$ was obtained using 3.60×10^{-5} M **12** and 0.142 M BzO^-.

arm.[18] The presence of two ureido functions in **12** strengthen the binding constant for planar NO_3^- anion by two orders of magnitude from 6.9×10^3 M^{-1} (model) to 3.9×10^5 M^{-1} (receptor **12**).

The spectral features of complexes allow distinguishing the binding mode of anions, *i.e.*, if anion is bound by four (between two ureas) or two (two hydrogens of one urea) hydrogen-bonding interactions. For example, the strong interaction of **12** (band at 333 nm, 3.1×10^4 M^{-1} cm^{-1}) with benzoates leads to a 1 : 1 complex characterized by the absorption band at 363 nm (Fig. 6 and 7(b)) where BzO^- interacts with the preorganised binding site of two ureas. At large excess of BzO^- the absorption band of the 1 : 1 complex further moves to longer wavelengths (*i.e.*, to 377 nm) indicating the transformation of the 1 : 1 stoichiometry to 1 : 2 where each urea of **12** binds BzO^- separately (Fig. 7(c)). This interpretation is corroborated by the spectral features of calixarene bearing only one urea-nitrophenyl arm[18] (two hydrogen bonding interactions are available): the original absorption band at 330 nm shifts to 380 nm upon forming the 1 : 1 complex with BzO^-, *i.e.* it has the similar position as the band of **12**·$(BzO^-)_2$.

Conclusions

Effective anion receptors **7–12** were obtained by the attachment of two urea moieties into the *para* positions of calix[4]arene immobilised in the *1,3-alternate* conformation. The substituents on the urea moiety heavily influence the binding ability of receptors. The presence of electron withdrawing groups (receptors **9** and **12**) results in very high binding affinity towards anions. The structural motif "aromate-urea-aromate" combined with the *1,3-alternate* conformation of the calix[4]arene skeleton proved to be very useful in design of novel anion receptors. The interdependence between the binding affinity and structural characteristics of binding sites provides a rational basis for the design and creation of novel receptors systems for molecular recognition.

Experimental

Melting points were determined on a Boetius block apparatus (Carl Zeiss Jena, Germany) and are not corrected. All ^1H NMR and ^{13}C NMR measurements were performed in 5 mm o.d. sample tubes and were recorded on a Varian Gemini 300 or Varian Mercury 300, using tetramethylsilane as an internal standard. Mass spectra were measured using the ESI technique on a Q-TOF (Micromass) spectrometer or the MALDI-TOF technique on an HP G2030A (Hewlett Packard) with a delayed extraction option. All UV/vis spectra were measured on a PerkinElmer Lambda 35 spectrometer. Crystal structures were determined by X-ray crystallography, data were collected on an Enraf Nonius CAD4 diffractometer with graphite monochromated Cu-Kα radiation at 293 K. The crystal structures presented in this paper were created using the *Platon for Windows*[14] *and POV-Ray™ for Windows, version 3.6*.

Dichloromethane used for the reactions was dried with CaH_2, and stored over 4 Å molecular sieves. The purity of the substances and the courses of reactions were monitored by TLC using TLC aluminum 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). All chemicals from Aldrich, Fluka, Merck, Lancaster and Across Organics with 99% and higher purity were used without further purification.

26,28-Dihexyloxy-5,17-dinitro-25,27-dipropoxy-calix[4]arene (*1,3-alternate*) 4 and (*partial cone*) 5

5,17-dinitro-25,27-dipropoxycalix[4]arene-26,28-diol **3** (1 g, 1.67 mmol) was stirred in anhydrous DMF (50 ml) with Cs_2CO_3 (3.84 g, 0.0118 mol). Then hexyl iodide (1.74 ml, 11.8 mmol) was added and the reaction mixture was heated to 110 °C for 5 days. The mixture was then spoiled into 1M HCl and extracted with chloroform. Traces of iodine were removed by washing with 20% Na_2SO_3 and organic layer was dried over anhydrous magnesium sulfate. The solvents were removed *in vacuo* and the crude mixture was resolved by column chromatography by CH_2Cl_2: petroleum ether 3 : 1 (v/v) as eluent. 26,28-Dihexyloxy-5,17-dinitro-25,27-dipropoxycalix[4]arene (*1,3-alternate*) **4** (R_F = 0.3) was obtained as yellowish powder in 17% yield (0.27 g), mp 152–155 °C. Found: C, 72.0; H, 7.6; N, 3.6 ($C_{46}H_{58}N_2O_8$ requires C 72.04; H 7.62; N 3.65). ^1H NMR (300 MHz; $CDCl_3$, 296 K): δ 7.82 (4H, s, Ar–H), 6.92 (4H, d, *J* 7.4, Ar–H), 6.64 (2H, t, *J* 7.4, Ar–H), 3.62–3.51 (16H, m, O–CH_2 + Ar–CH_2–Ar), 1.66–1.58 (8H, m, 4 × CH_2), 1.28 (12H, m, 6 × CH_2), 0.88 (12H, m, 4 × –CH_3); ^{13}C NMR (75 MHz; $CDCl_3$, 296 K): δ 161.8, 156.0, 141.4, 134.4, 132.3, 130.1, 125.1, 121.9, 73.7, 72.7, 35.9, 31.6, 30.2, 25.4, 23.2, 22.5, 13.9 and 10.1; TOF-MS ESI+ required 766.4 for $C_{46}H_{58}N_2O_8$, found: 789.6 $[M + Na]^+$ (100%).

Partial cone analogue **5** (R_F = 0.9) was obtained as yellowish microcrystals in 70% yield (1.11 g), mp 158–160° C. Found: C, 71.9; H, 7.6; N, 3.6 ($C_{46}H_{58}N_2O_8$ requires C 72.04; H 7.62; N 3.65). ^1H NMR (300 MHz; $CDCl_3$, 296 K): δ 8.22 (2H, s, Ar–H), 8.03 (2H, s, Ar–H), 6.92 (2H, d, *J* 6.7, Ar–H), 6.47 (2H, t, *J* 7.4, Ar–H), 6.25 (2H, d, *J* 7.0, Ar–H), 4.11 (2H, d,

J 12.9, Ar–CH_2–Ar), 3.90 (2H, t, *J* 7.2, O–CH_2), 3.84–3.65 (6H, m, 2 × O–CH_2 + Ar–CH_2–Ar), 3.58 (2H, t, *J* 7.2, O–CH_2), 3.44 (2H, t, *J* 7.7, O–CH_2), 3.19 (2H, d, *J* 13.5, Ar–CH_2–Ar), 2.02–1.93 (6H, m, 3 × O–CH_2–CH_2), 1.54–1.46 (2H, m, O–CH_2–CH_2), 1.44–1.32 (6H, m, 3 × CH_2), 1.24–1.31 (2H, m, CH_2), 1.23–1.14 (2H, m, CH_2), 1.12 (6H, t, *J* 7.2, 2 × –CH_3), 1.07–0.96 (2H, m, CH_2), 0.95 (3H, t, *J* 7.2, –CH_3), 0.89 (3H, t, *J* 7.7, –CH_3); ^{13}C NMR (75 MHz; $CDCl_3$, 296 K): δ 163.7, 156.0, 142.9, 142.5, 138.4, 135.5, 132.5, 131.4, 129.9, 129.3, 126.2, 124.8, 122.5, 76.8, 75.0, 74.3, 35.4, 31.6, 31.2, 30.7, 30.5, 28.7, 25.6, 24.9, 23.6, 22.7, 22.5, 13.8, 13.7 and 10.6; TOF-MS ESI+ required 766.4 for $C_{46}H_{58}N_2O_8$, found: 789.4 $[M + Na]^+$ (100%).

5,17-Diamino-26,28-dihexyloxy-25,27-dipropoxy-calix[4]arene (*1,3-alternate*) 6

Dinitro-derivative **4** (0.27 g, 0.35 mmol) was dispersed in 25 ml of ethanol. Then $SnCl_2{\cdot}2H_2O$ (0.79 g, 3.5 mmol) was added and the mixture was heated to reflux overnight. Solvent was evaporated, the residue was taken up with chloroform and poured into 1 M KOH. The product was extracted into chloroform, combined organic layers were washed once with brine and then evaporated to dryness, yielding 0.22 g of **6** (89%), mp 83–85° C. Found: C, 78.1; H, 8.8; N, 4.0 ($C_{46}H_{62}N_2O_4$ requires C 78.15; H 8.84; N 3.96). ^{1}H NMR (300 MHz; $CDCl_3$, 296 K): δ 7.26 (4H, s, NH_2), 6.97 (4H, d, *J* 7.4, Ar–H), 6.63 (2H, t, *J* 7.4, Ar–H), 6.49 (4H, s, Ar–H), 3.55–3.50 (16H, m, O–CH_2 + Ar–CH_2–Ar), 1.72 (4H, m, 2 × CH_2), 1.61 (4H, m, 2 × CH_2), 1.35 (12H, m, 6 × CH_2), 1.01 (6H, t, 2 × –CH_3), 0.88 (6H, t, 2 × –CH_3); ^{13}C NMR (75 MHz; $CDCl_3$, 296 K): δ 156.4, 149.9, 140.9, 134.4, 133.8, 129.8, 121.7, 117.8, 74.8, 73.3, 36.3, 32.2, 30.4, 26.0, 23.8, 22.9, 14.8, 11.9; TOF-MS ESI+ required 706.5 for $C_{46}H_{62}N_2O_4$, found: 729.7 $[M + Na]^+$ (100%).

Synthesis of 5,17-bisureido derivatives 7–12. General procedure

5,17-Diaminocalix[4]arene **6** (0.1 g, 0.14 mmol) was stirred in anhydrous dichloromethane (10 ml) under the atmosphere of dry nitrogen. The corresponding isocyanate (1.6 mmol) was added and the reaction mixture was stirred overnight at room temperature. The reaction was quenched by the addition of methanol (30 ml) and the precipitate (crude product) was filtered off. The purification methods are described for each particular ligand below.

5,17-Bis(*N′*-phenylureido)-26,28-dihexyloxy-25,27-dipropoxycalix-[4]arene (*1,3-alternate*) 7[6i]

No further purification was needed and the product **7** was isolated as a white solid in 55% yield, mp 233–235 °C. Found: C, 76.2; H, 7.7; N, 5.8 ($C_{60}H_{72}N_4O_6$ requires C 76.24; H 7.68; N 5.93); ^{1}H NMR (300 MHz; $CDCl_3$, 296 K): δ 7.91 (2H, s, NH), 7.50 (4H, d, *J* 7.7, Ar–H), 7.32 (4H, m, Ar–H), 7.05 (2H, t, *J* 7.7, Ar–H), 7.00–6.97 (8H, m, Ar–H), 6.63 (2H, t, *J* 7.3, Ar–H), 6.46 (2H, s, NH), 3.68–3.63 (8H, m, O–CH_2–), 3.52 (8H, s, Ar–CH_2–Ar), 1.80–1.73 (8H, m, 4 × CH_2), 1.57 (8H, m, 4 × CH_2), 1.42 (4H, m, 2 × CH_2), 0.96 (6H, t, *J* 7.4, 2 × CH_3), 0.87 (6H, t, *J* 7.3, 2 × CH_3); ^{13}C NMR (75 MHz; $CDCl_3$, 296 K): δ 155.7, 154.5, 153.8, 139.2, 135.2, 133.4, 131.3, 130.1, 129.1, 124.5, 123.3, 122.4, 119.8, 75.6, 73.6, 35.3, 32.1, 30.7, 26.1, 24.2, 22.9, 14.3, 10.8; TOF-MS ESI+ required 944.6 for $C_{60}H_{72}N_4O_6$, found: 967.5 $[M + Na]^+$ (100%).

5,17-Bis(*N′*-benzylureido)-26,28-dihexyloxy-25,27-dipropoxy-calix[4]arene (*1,3-alternate*) 8

The crude product was purified by preparative TLC ($CHCl_3$–ethyl acetate 15 : 1) to obtain pure compound **8** as a white powder in 63% yield, mp 246–248 °C. Found: C, 76.4; H, 7.8; N, 5.7 ($C_{62}H_{76}N_4O_6$ requires C 76.51; H 7.87; N 5.76); ^{1}H NMR (300 MHz; $CDCl_3$, 296 K): δ 7.36–7.28 (10H, m, ArH), 6.96 (4H, d, *J* 7.4, Ar–H), 6.91 (4H, s, Ar–H), 6.57 (2H, t, *J* 7.5, Ar–H), 6.28 (2H, s, NH), 6.06 (2H, t, CH_2–N*H*), 4.50 (4H, d, *J* 5.8, CH_2–NH), 3.70–3.28 (8H, m, O–CH_2–), 3.44 (8H, m, Ar–CH_2–Ar), 1.91–1.83 (8H, m, 4 × CH_2), 1.58–1.40 (12H, m, 6 × CH_2), 1.05 (6H, t, *J* 7.1, 2 × CH_3), 0.96 (6H, t, *J* 6.9, 2 × CH_3); ^{13}C NMR (75 MHz; $CDCl_3$, 296 K): δ 157.1, 155.7, 153.5, 139.2, 134.9, 133.4, 131.5, 130.0, 128.7, 127.6, 127.3, 124.4, 122.2, 75.5, 73.6, 44.2, 35.2, 32.1, 30.7, 26.1, 24.1, 22.9, 14.3, 10.9; TOF-MS ESI+ required 972.6 for $C_{62}H_{76}N_4O_6$, found: 995.6 $[M + Na]^+$ (100%), 973.5 $[M + H]^+$ (30%).

5,17-Bis[*N′*-(phenylsulfonyl)ureido]-26,28-dihexyloxy-25,27-dipropoxycalix[4]arene (*1,3-alternate*) 9

The crude product was purified by column chromatography (CH_2Cl_2–ethyl acetate 5 : 1). The product **9** was obtained as a yellowish solid in 66% yield, mp 215–217 °C. Found: C, 67.1; H, 6.6; N, 5.1; S 5.9 ($C_{60}H_{72}N_4O_{10}S_2$ requires C 67.14; H 6.76; N 5.22; S 5.97); ^{1}H NMR (300 MHz; $CDCl_3$, 296 K): δ 8.05 (4H, d, *J* 7.7, Ar–H), 7.67 (6H, m, Ar–H), 7.03 (4H, d, *J* 7.5, Ar–H), 6.95 (4H, s, Ar–H), 6.77 (2H, t, *J* 7.2, Ar–H), 3.71–3.57 (16H, m, 4 × O–CH_2– + Ar–CH_2–Ar), 1.79 (4H, m, 2 × CH_2), 1.62 (4H, m, 2 × CH_2), 1.32 (12H, m, 6 × CH_2), 0.96 (6H, t, *J* 7.1, 2 × CH_3), 0.94 (6H, t, *J* 7.1, 2 × CH_3); ^{13}C NMR (75 MHz; $CDCl_3$, 296 K): δ 150.7, 139.6, 138.3, 134.1, 133.2, 132.9, 131.2, 129.2, 129.1, 128.9, 128.4, 128.2, 126.5, 77.2, 75.3, 53.7, 31.9, 29.7, 25.6, 23.5, 22.7, 14.1, 10.1; TOF-MS ESI+ required 1072.5 for $C_{60}H_{72}N_4O_{10}S_2$, found: 1095.4 $[M + Na]^+$ (100%)

5,17-Bis(*N′*-benzoylureido)-26,28-dihexyloxy-25,27-dipropoxy-calix[4]arene (*1,3-alternate*) 10

The crude product was purified by preparative TLC chromatography ($CHCl_3$–ethyl acetate 3 : 1) and crystallized from acetonitrile to give **10** as white crystals in 36% yield, mp. 249–250 °C. Found: C, 74.3; H, 7.2; N, 5.5 ($C_{62}H_{72}N_4O_8$ requires C 74.37; H 7.25; N 5.60); ^{1}H NMR (300 MHz; $CDCl_3$, 296 K): δ 10.92 (2H, s, NH), 10.49 (2H, s, NH), 8.05 (4H, d, *J* 7.2, Ar–H), 7.60–7.42 (6H, m, Ar–H), 7.24 (4H, s, Ar–H), 7.01 (4H, d, *J* 7.4, Ar–H), 6.72 (2H, t, *J* 7.7, Ar–H), 3.67 (4H, d, *J* 14.6, Ar–CH_2–Ar), 3.55 (4H, d, *J* 14.9, Ar–CH_2–Ar), 3.43 (4H, t, 2 × O–CH_2–), 3.17 (4H, t, 2 × O–CH_2–), 1.54 (4H, m, 2 × CH_2), 1.31–1.26 (16H, m, 8 × CH_2), 0.95 (6H, m, 2 × CH_3), 0.64 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz; $CDCl_3$, 296 K): δ 168.8, 156.7, 153.2, 152.0, 134.3, 133.8, 132.9, 132.5, 131.1, 130.1, 128.6, 128.3, 121.6, 121.1, 71.9, 71.5, 37.6, 32.0, 30.2, 25.6, 22.7, 22.6, 14.2, 9.1;

TOF-MS ESI+ required 1000.5 for $C_{62}H_{72}N_4O_8$, found: 1023.3 $[M + Na]^+$ (100%).

5,17-Bis(*N*′-chloroacetylureido)-26,28-dihexyloxy-25,27-dipropoxycalix[4]arene (*1,3-alternate*) 11

The precipitated solid was filtered off and washed twice with methanol to yield pure compound **11** in 69% yield, mp >300 °C. Found: C, 65.9; H, 6.9; Cl, 7.4; N, 5.9 ($C_{52}H_{66}Cl_2N_4O_8$ requires C 66.02; H 7.03; Cl 7.50; N 5.92); ^{1}H NMR (300 MHz; $CDCl_3$, 296 K): δ 9.86 (2H, s, NH), 8.73 (2H, s, NH), 7.16 (4H, s, Ar–H), 6.99 (4H, d, J 7.7, Ar–H), 6.69 (2H, t, J 7.5, Ar–H), 4.19 (4H, s, –CH_2Cl), 3.64 (8H, s, Ar–CH_2–Ar), 3.56 (4H, t, J 7.9, 2 × O–CH_2–), 3.49 (4H, t, J 6.6, 2 × O–CH_2–), 1.61 (4H, m, 2 × CH_2), 1.50 (4H, m, 2 × CH_2), 1.30 (12H, m, 6 × CH_2), 0.93 (6H, t, J 6.3, 2 × CH_3), 0.87 (6H, t, J 6.9, 2 × CH_3); ^{13}C NMR (75 MHz; $CDCl_3$, 296 K): δ 168.5, 167.7, 156.8, 154.2, 149.8, 134.5, 133.5, 129.9, 122.4, 121.9, 73.3, 72.0, 42.7, 37.1, 32.1, 30.2, 25.8, 23.5, 22.8, 14.3, 10.4; TOF-MS ESI+ required 944.4 for $C_{52}H_{66}Cl_2N_4O_8$, found: 967.4 $[M + Na]^+$ (100%).

5,17-Bis[*N*′-(4-nitrophenyl)ureido]-26,28-dihexyloxy-25,27-dipropoxycalix[4]arene (*1,3-alternate*) 12

The product was purified by preparative TLC chromatography ($CHCl_3$) and then crystallized from acetonitrile. The pure product **12** was obtained as yellow crystals in 71%, mp 199–202 °C. Found: C, 69.5; H, 6.7; N, 8.0 ($C_{60}H_{70}N_6O_{10}$ requires C 69.61; H 6.82; N 8.12); ^{1}H NMR (300 MHz; $CDCl_3$, 296 K): δ 9.48 (2H, s, NH), 8.68 (2H, s, NH), 8.28 (4H, d, J 9.0, Ar–H), 7.76 (4H, d, J 9.0, Ar–H), 6.99 (8H, m, Ar–H), 6.82 (2H, t, J 7.4, Ar–H), 3.72 (8H, s, Ar–CH_2–Ar), 3.57–3.49 (8H, m, 4 × CH_2), 1.78 (4H, m, 2 × CH_2), 1.51 (4H, m, 2 × CH_2), 1.49–1.25 (12H, m, 6 × CH_2), 0.95 (6H, t, J 6.6, 2 × CH_3), 0.29 (6H, t, J 7.2, 2 × CH_3); ^{13}C NMR (75 MHz; $CDCl_3$, 296 K): δ 179.8, 156.3, 149.3, 145.3, 143.9, 136.5, 133.0, 131.2, 131.1, 126.9, 124.4, 123.7, 122.9, 74.9, 71.3, 37.2, 31.9, 29.5, 25.5, 23.3, 22.7, 14.1, 10.0; TOF-MS ESI+ required 1034.5 for $C_{60}H_{70}N_6O_{10}$, found: 2092.8 $[2M + Na]^+$ (10%), 1057.7 $[M + Na]^+$ (100%), $[M + H]^+$ 1035.7 (15%). UV/Vis (CH_2Cl_2): λ_{max}/nm (ε/M^{-1} cm^{-1}): 333 (3.05×10^4).

Crystallography

Crystal data for **10**: $C_{62}H_{72}N_4O_8$, M = 1001.3 g mol^{-1}, triclinic, space group $P2_1/n$, a = 11.2715(9), b = 19.3820(7), c = 25.918(2) Å, β = 99.967(6)°, V = 5577.0(6) Å^3, Z = 4, D_c = 1.19 g cm^{-3}, μ(Cu-Kα) = 1.87 mm^{-1}, crystal dimensions of 0.4 × 0.5 × 0.9 mm. The structure was solved by the direct method[15] and all heavy atoms except the alkoxy chains were refined anisotropically by full-matrix least squares on F values[16] to final R = 0.0825 and R_w = 0.0822 using 3643 independent reflections (θ_{max} = 69.91°, 577 parameters). Carbon atoms in the alkoxy groups were refined only isotropically, no geometrical restrains were applied to these groups. Hydrogen atoms on carbon atoms were located from an expected geometry and were not refined, N–H hydrogen atoms were located from differential electron density maps. ψ-scan was used for absorption correction.

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