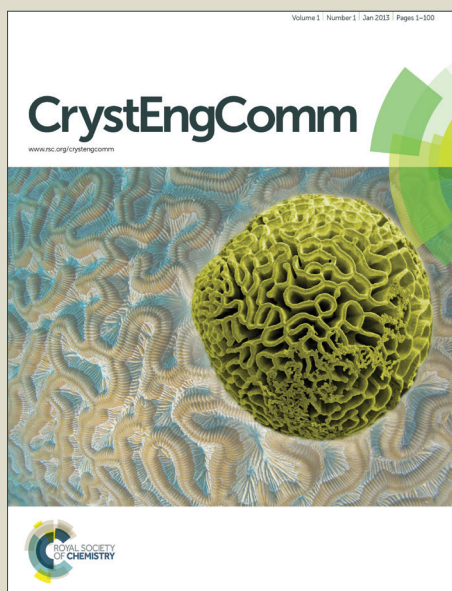


CrystEngComm

Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

ARTICLE

Hydrogen Bonding Effects in Anion Binding Calixarenes

Cite this: DOI: 10.1039/x0xx00000x

Naseem Qureshi,^a Dimitri S. Yufit,^b Kirsty M. Anderson,^b Judith A. K. Howard^b and Jonathan W. Steed^{*b}

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

A series of disubstituted urea, thiourea and dansyl amide calix[4]arene based anion receptors have been prepared and characterised by X-ray crystallography. The structures show a fine balance of intramolecular urea α -tape, and urea...calixarene phenolic oxygen atom hydrogen bonding patterns. Both motifs are in competition with the anion binding behaviour of the compounds in solution.

Introduction

Calixarenes have been used extensively as scaffolds for enzyme mimics,¹ HCl co-transporters,² and receptors for cationic, anionic and neutral guests.³⁻⁹ As part of their work on calixarene-based membrane transporters and chemically modified field effect transistors (CHEMFETs) the Reinhoudt group developed a range of lipophilic di- and tetra(urea) calix[4]arene receptors of type **1** and **2**¹⁰ displaying significant selectivity for the biologically important^{11, 12} chloride anion. Analogous tris(urea) calix[6]arenes are selective for tricarboxylates.¹³ Monte Carlo modelling by Jorgensen and co-workers on the 1,3-difunctionalised bis(urea) calix[4]arene **1** (R = Ph) in which the urea groups are linked to the calixarene phenolic oxygen atoms by relatively long, flexible butylene spacers, suggests that the compound adopts a conformation involving an intramolecular urea-urea six-membered-ring hydrogen bond,¹⁴ $R_2^1(6)$ in graph set nomenclature¹⁵ (Fig. 1a). Chloride binding then disrupts this interaction and the anion is bound in a cleft between the pair of urea functional groups (Fig. 1d). Subsequent X-ray crystallographic analysis on the related bis(thiourea) derivative **3a** which possesses shorter ethylene linkers and no alkyl substituents on the calixarene 2- and 4-position phenolic rings, reveals intramolecular OH...O interactions at the narrow ('lower') rim, intramolecular NH...O interactions from thiourea to phenolic oxygen (Fig. 1c) and intermolecular thiourea hydrogen bonding of the $R_2^2(8)$ type (Fig. 1b).¹⁶ A range of other more conformationally constrained cyclic calix[4]- and calix[6]arene derivatives has also been produced based in the pendant urea or thiourea template.¹⁷⁻²¹ The presence of OH...O hydrogen bonding at the lower rim in calixarenes is known to rigidify the cone conformation²² and hence potentially preorganise the anion binding pocket provided by the urea pendant groups. Additional preorganisation may also be offered by the shorter, less flexible ethylene spacer groups in **3a** as opposed to the longer butylene groups in compounds such as **1**. However, a shorter linker may also favour the hydrogen bonding involving intramolecular interactions between one of the thiourea or urea NH groups (in

an *cis* conformation²³ with respect to the urea carbonyl) and the calixarene oxygen atoms, as shown in Fig. 1c. In order to probe the occurrence of these various hydrogen bonding modes and examine their influence on anion, and specifically chloride, affinity in these systems we have prepared the disubstituted pendant bis(urea) calix[4]arenes **3b** and **4a-c**. We now report their structural and anion binding characteristics, along with their dansyl analogues **5** and **6**, which are designed as act as fluorescent chloride anion sensors.

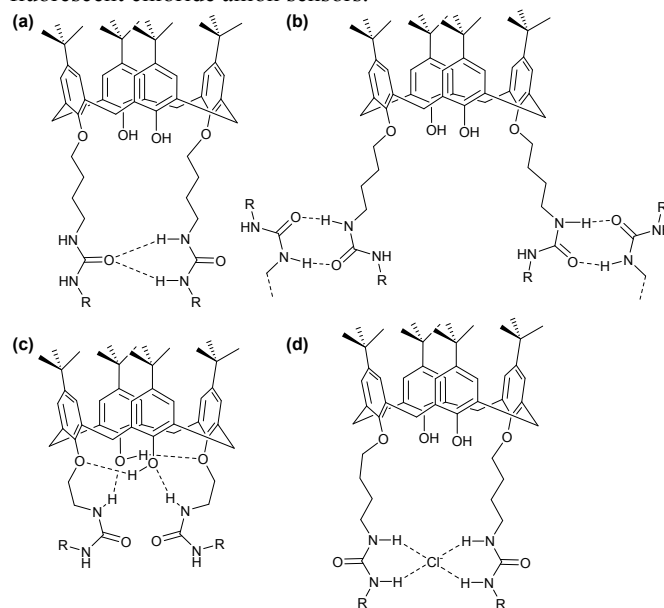


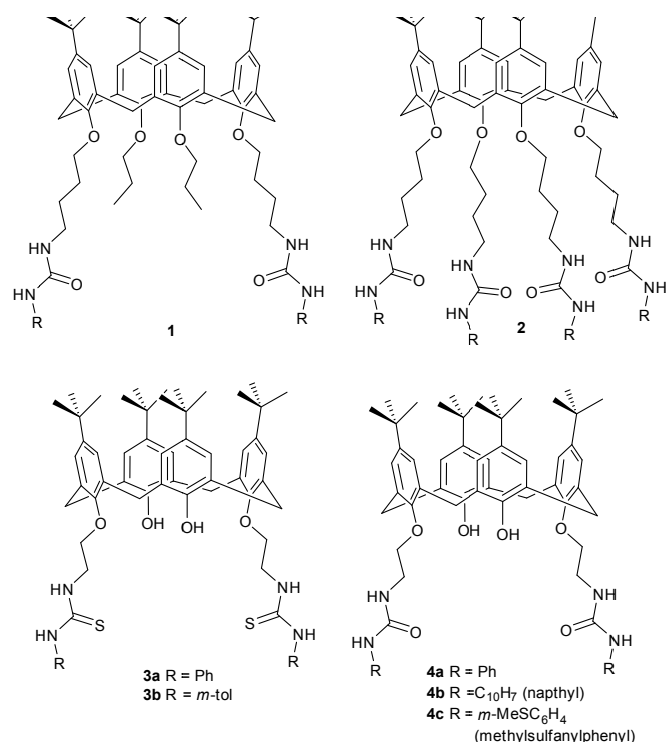
Figure 1: Hydrogen bonding modes in bis(urea) calixarenes (a) intramolecular urea $R_2^1(6)$, (b) intermolecular $R_2^2(8)$, (c) amide or urea-calixarene $R_2^2(7)$, (d) urea-chloride double $R_2^1(6)$.

Results and discussion

Bis(urea) Calixarenes

Disubstituted bis(urea) calixarenes of type **4** were prepared from reaction of the appropriate isocyanate with the known calixarene bis(2-aminoethyl) derivative.²⁴ During the course of this work a variety of nitrile intermediates were also characterised by X-ray crystallography – see supplementary information. Anion binding studies in acetone and chloroform solution with the *p*-tolyl derivative **4a** proved to be disappointing. Compound **4a** showed evidence for fluxional behaviour on the NMR spectroscopic timescale and exhibited poor solubility. As a result we turned our attention to compounds **4b** and **4c**.

Crystals of **4b** suitable for X-ray diffraction were obtained from acetonitrile/chloroform solution and proved to be of the mixed acetonitrile/chloroform solvate **4b**·2MeCN·2CHCl₃. The molecular structure shows the expected 1,3-disubstitution pattern and a pinched cone conformation.^{25, 26} The calixarene cavity is occupied by one of the lattice acetonitrile molecules.



The structure exhibits intramolecular hydrogen bonding interactions involving the calixarene hydroxyl groups to the adjacent phenolic oxygen atoms (2.91 and 2.95 Å) as shown in Fig. 2a. The urea groups adopt an unusual *cis-trans* conformation²³ (as opposed to the expected *trans-trans* conformation compatible with urea α -tape hydrogen bonding²⁷) and are involved in two different intermolecular modes of interaction. One urea group forms an intermolecular hydrogen bonding interaction of the $R_2^2(8)$ type (Fig. 1b). The other forms a single, long and rather bent NH $\cdots$ O=C interaction (N $\cdots$ O 3.07 Å) to another urea group on a further molecule (Fig. 2b). The carbonyl oxygen atom of this urea acts as an acceptor for a CH $\cdots$ O hydrogen bond from an included molecule of acetonitrile. The urea α -NH protons of both unique urea groups also form intramolecular interactions to the calixarene phenolic oxygen atoms (Fig. 1c and Fig. 2a). While this *cis-trans* arrangement and formation of the $R_2^2(8)$ motif is analogous to the thiourea derivative **3a**, the absence of the

$R_2^1(6)$ motif is unusual in the oxygen analogues and may arise from the dominance of an intramolecular interaction to the calixarene oxygen atoms, facilitated by the short ethylene spacer. The complex crystal packing arrangement also involves offset π - π interactions between the naphthyl groups on adjacent calixarenes and CH $\cdots$ π interactions involving the included chloroform, as well as intramolecular π -interactions to the calixarene aromatic rings.²⁸ Overall it seems evident that the intramolecular interactions shown in Fig 2a bring about the unusual *cis-trans* urea conformation resulting in a complex series of intermolecular interactions for the urea β -NH protons. (a)

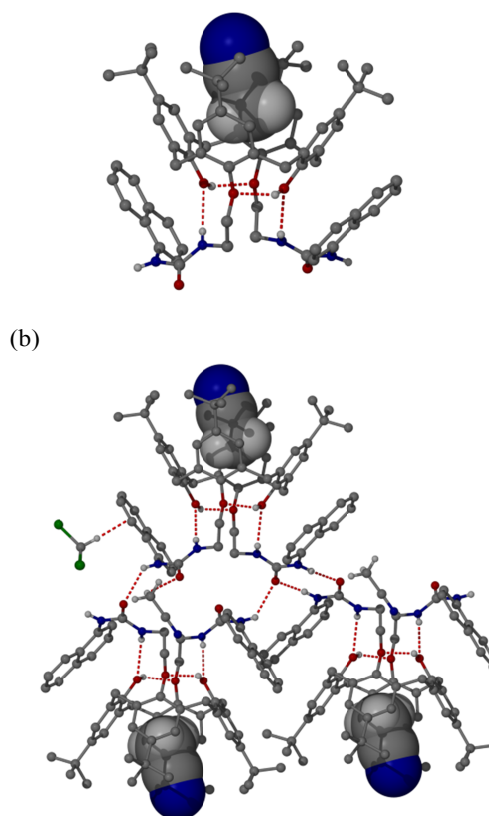


Figure 2: X-ray crystal structure of **4b**·2MeCN·2CHCl₃ showing (a) the $R_2^1(6)$ intramolecular hydrogen bonding and (b) the intermolecular $R_2^2(8)$ motif. CH hydrogen atoms omitted for clarity. Acetonitrile intracavity guests shown in spacefilling mode.

The methylsulfanylphenyl derivative **4c** was also characterised by X-ray crystallography as a mixed acetone/methanol solvate of formula **4c**·1.5OCMe₂·0.5MeOH. The cavity is occupied by an acetone guest and the calixarene displays a pinched cone conformation with two intramolecular OH $\cdots$ O interactions from the calixarene phenolic groups, as observed for **4b**. However, remarkably, the urea groups do not associate with the calixarene phenolic oxygen atoms and instead form the conventional urea α -tape type $R_2^1(6)$ motif (Fig. 3), analogous to the geometry calculated for **1** (R = Ph) by Monte Carlo methods.¹⁴ The calculations for **1** suggest an unsymmetrical six-membered ring with the NH group closest to the calixarene forming a markedly shorter hydrogen bond to the adjacent urea carbonyl group.¹⁴ In the present experimental structure of **4c** the six-membered hydrogen bonded ring is

relatively symmetrical and it is the distal urea NH group that forms the slightly shorter interaction; N $\cdots$ O=C distances 3.07 and 2.89 Å. However, these distances are likely to be dominated by crystal packing effects in these flexible compounds. The significant differences in the structures of **4b** and **4c** are not obviously related to the differences in the urea substituent groups and suggest that the alternative hydrogen bonding modes, and hence urea conformations, are finely balanced in this system in contrast to the usual predominance of the α -tape $R_2^1(6)$ arrangement,²⁷ and are likely heavily influenced by crystal packing factors.

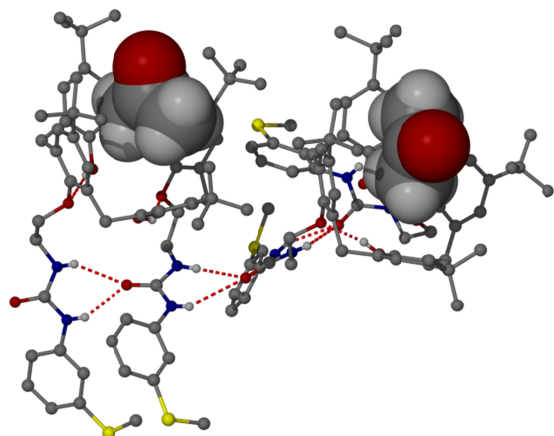


Figure 3: Urea $R_2^1(6)$ tape hydrogen bonding in the structure of **4c**. CH hydrogen atoms omitted for clarity. Intracavity guests shown in space-filling mode.

The anion binding properties of receptors **4b** and **4c** were examined in acetone solution using ^1H NMR spectroscopic titration. Significant chemical shift changes were observed on titration of both receptors with tetrabutylammonium chloride, bromide, acetate and nitrate. In the case of the interaction of **4c** with Cl^- , anion binding is evident in the chemical shift changes in the NH and OH resonances, initially at 8.31 and 8.65 ppm. The NH resonance moves downfield ($\Delta\delta = 1.72$ ppm) giving a clean titration isotherm which can be readily fit to a 1:1 stoichiometric model. In contrast, the OH resonance undergoes a much less significant upfield chemical shift change ($\Delta\delta = -0.27$ ppm after addition of one equivalent of anion). It is likely that the $\text{OH}\cdots\text{O}$ intramolecular hydrogen bonding at the calixarene narrow rim is retained in the chloride complex, while the urea intramolecular hydrogen bonding interaction observed in the crystal structure is replaced by a number of $\text{NH}\cdots\text{Cl}^-$ hydrogen bonds.^{29, 30} The $\text{OH}\cdots\text{O}$ interaction apparently becomes weaker as the conformation of the calixarene adapts to accommodate the anion guest. The second NH peak also undergoes a marked chemical shift change but becomes obscured by other resonances during the course of the titration. In the case of titration with acetate anion the chemical shift change is even more marked ($\Delta\delta = 2.63$ and -0.32 ppm for the NH and OH resonances, respectively). Similar behaviour in terms of magnitude and direction of chemical shift changes were observed for the naphthyl derivative **4b**. Fitting the titration isotherm using HypNMR 2006^{31, 32} yields the association constants given in Table 1. For **4c** the selectivity order is $\text{Cl}^- > \text{OAc}^- > \text{NO}_3^- > \text{Br}^-$ and hence the receptor is weakly chloride selective. Receptor **4b** exhibits generally slightly lower affinity, perhaps because of the intramolecular hydrogen bonding interactions to the calixarene oxygen atoms.

Table 1: Anion binding constants ($\log \beta_{11}$, NBu_4^+ salts) for new receptors in acetone at 20 °C

Receptor	Anion			
	Cl^-	Br^-	OAc^-	NO_3^-
4b	3.59(4)	-	-	2.38(8)
4c	3.91(3)	3.41(3)	3.76(4)	3.03(1)

Moving from urea ($\text{X}=\text{O}$) to thiourea ($\text{X}=\text{S}$) results in an increase in the $\text{C}=\text{X}$ bond length and hence generally the observation of $R_2^2(8)$ type hydrogen bonding patterns instead of the urea α -tape $R_2^1(6)$ motif.^{27, 33, 34} This propensity is observed in the $R_4^4(14)$ intramolecular hydrogen bonding, and $R_2^2(8)$ intermolecular ribbon formation observed in the structure of thiourea derivative **3a** (Fig. 1b and 1c).¹⁶ In general we anticipate that thiourea derivatives should favour this arrangement in contrast to the structure of **4c** because of the longer $\text{C}=\text{S}$ bond. By way of confirmation we prepared a close analogue of **3a**, the bis(*m*-tolylurea) derivative **3b**. This compound was also structurally characterised as the mixed chloroform/ethanol solvate and adopts a conformation closely related to **3a**, exhibiting an *cis-trans* conformation of the thiourea moieties. While the thiourea groups adopt an intramolecular $R_4^4(14)$ interaction to the calixarene oxygen atoms analogous to **4b**, the expected intermolecular $R_2^2(8)$ ribbon analogous to **3a** is absent and is replaced by a solvent separated hydrogen bonded ring of graph set $R_4^4(12)$ involving two well-ordered ethanol molecules (Fig. 4). The calixarene cavity is occupied by a disordered combination of ethanol and chloroform. While the details of the packing are thus rather different to the closely related **3a** the dominance of intramolecular over intermolecular hydrogen bonding is consistent with the structure of **3a** and **4b** and is in contrast to the urea α -tape structure of **4c**.

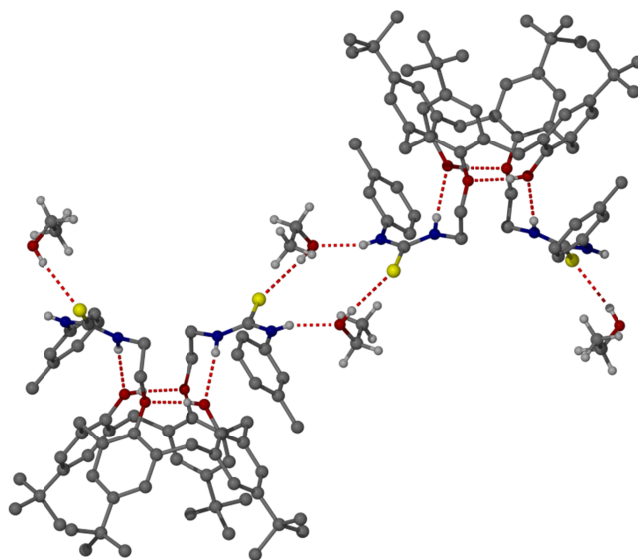


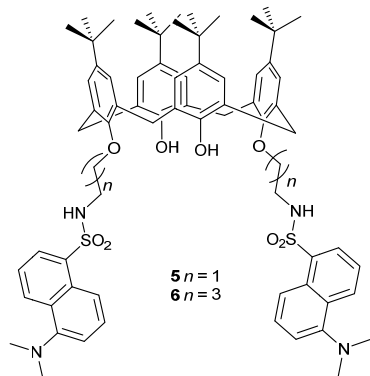
Figure 4: X-ray crystal structure of bis(*m*-tolylurea) derivative **3b** showing the intermolecular ethanol solvent-separated hydrogen bonded ribbon and an intramolecular $R_4^4(14)$ interaction to the calixarene oxygen atoms. Calixarene CH hydrogen atoms omitted for clarity.

Due to increased acidity of the NH protons of the thiourea compared to urea (thiourea $\text{pK}_a = 21.0$; urea $\text{pK}_a = 26.9$),³⁵ the

anion complexation ability of the thiourea derivative was expected to be stronger. The increased acidity is evident from the ^1H -NMR spectrum of **3b** where the NHb proton is shifted 0.26 ppm and the NHa proton 0.57 ppm to lower field compared to the urea analogue **4a**. ^1H -NMR spectroscopic titration experiments were performed with TBA^+X^- ($\text{X} = \text{Cl}, \text{OAc}, \text{NO}_3$) in acetone- d_6 . The ^1H -NMR resonances assigned to NHa, OH and NHb occur at 7.87, 8.08 and 6.75 ppm in the free host. The urea NHa proton shifts to 9.32 ppm ($\Delta\delta = 1.45$ ppm) upon 1:1 chloride binding, $\log \beta_{11} = 3.16(6)$. The OH peak moves from 8.08 ppm to 8.27 ppm ($\Delta\delta = 0.19$ ppm). This chemical shift change is in the opposite direction to that observed for the oxygen analogues and suggests that intramolecular hydrogen bonding reinforces anion binding in this case. In the case of acetate anion, the NH resonances disappear suggesting deprotonation. The nitrate anion binds very weakly with chemical shift changes of the NH resonances still occurring on with addition of up to five equivalents of anion.

Dansylamide Derived Calixarenes

Given the affinity and modest chloride selectivity observed for receptors of type **4b** and **4c** we prepared the related dansyl amides **5** and **6** with, respectively, ethylene and butylene spacer groups linking the anion binding amide group with its appended chromophore to the calixarene scaffold. Compound **5** was characterised by X-ray crystallography which confirms that the dansylamide groups are substituted at 1,3-distal calixarene phenolic rings. The amide NH groups form a short intramolecular hydrogen bond (2.97 Å) to the oxygen atoms of the lower rim of the calixarene in a similar way to the structures of **3a**, **3b** and **4b** but in contrast to **4c** (Fig. 5). ^1H NMR spectroscopic titration of host **5** with TBA^+X^- ($\text{X} = \text{Cl}, \text{OAc}, \text{Br}, \text{F}, \text{NO}_3$) in a range of solvents did not produce any significant chemical shift change, suggesting that the amide functionalities may be unavailable for interaction with guest anions as a result of the intramolecular hydrogen bonding interaction. In contrast, ^1H NMR spectroscopic titration of host **7** bearing the longer butylene spacer gave a significant anion response. That fact that the ethylene-linked amide produces no anion binding response while the ethylene-linker ureas do bind anions may be attributed to the additional NH hydrogen bond donor in the ureas.



Titration with chloride in acetone- d_6 resulted in a shift in the NH peak from 6.83 ppm in the free host to 8.13 ppm at five equivalents. Other anion guests (OAc^- , Br^- , F^- and NO_3^-) have significantly less effect. Fitting the binding isotherm to a 1:1 model gave a relatively modest chloride binding constant of $\log \beta_{11} = 1.47(1)$, reflecting the single NH hydrogen bonding group of the amide as opposed to two NH groups of the urea moieties. However, the longer butylene spacer clearly disfavors the intramolecular hydrogen bonding and allows the compound to function as an anion receptor.

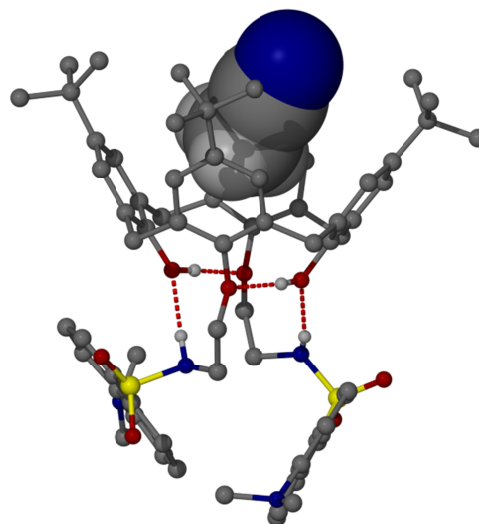


Figure 5: X-ray crystal structure of dansyl derivative **5** showing the intramolecular $R_4^4(14)$ interaction to the calixarene oxygen atoms. Intracavity acetonitrile guest shown in space-filling mode. Calixarene CH hydrogen atoms omitted for clarity.

The fluorescent response to chloride in compounds **5** and **6** was monitored by fluorescence titration in acetonitrile solution (see supplementary information figures S14 and S15). Both receptors are highly quenched in this medium, perhaps as a result of photo-induced electron transfer from the sulfonamide lone pair, even though this lone pair is expected to be delocalised. Addition of chloride results in significant fluorescence enhancement of the unstructured dansylamide monomer emission band in both compounds. For compound **5** there is no shift in the λ_{max} 514 nm upon anion addition up to 500 molar equivalents and Cl^- . For the butylene complex **6** the emission enhancement is accompanied by a shift in the wavelength of the monomer emission band from 511 nm to 520 nm consistent with the chloride binding by this compound observed by NMR spectroscopy. Emission enhancement on anion binding has been observed in intramolecularly hydrogen bonded dansyl-based receptors for cyanide,³⁶ however anion-induced quenching has been observed in other systems^{37, 38} including calixarene-based hosts for *N*-acetyl aspartate.³⁹ The origins of the emission enhancement in both compounds is difficult to explain, particularly given the very weak binding of chloride anion by **5**, but may reflect a change in the bulk ionic strength of the medium. The quantum yield of the dansyl

moiety is known to be highly dependent on the medium in ways that are not fully understood.⁴⁰ Recent work has also shown that aggregation-induced emission can result in enhancement of dansyl fluorescence, however this is accompanied by a significant shift in emission wavelength.⁴¹ Analogous titration with bromide, nitrate and acetate resulted in similar enhancement, with a shoulder appearing to lower wavelength in the case of acetate.

Conclusions

Intramolecular hydrogen bonding effects of both urea-to-urea and urea- or amide to calixarene types are in competition with

$\lambda = 0.71073 \text{ \AA}$). The standard data collection temperature was 120 K, maintained using an open flow N₂ Cryostream (OxfordCryosystems) device. Integration was carried out using the Bruker SAINT and Rigaku FS Process packages. Data sets were corrected for Lorentz and polarisation effects and for the effects of absorption. Structures were solved using direct methods and refined by full-matrix least squares on F² for all data using SHELXTL software.⁴³ All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were located on the difference Fourier map and refined isotropically. Molecular graphics were produced using the programs X-Seel and POV-Ray.^{44, 45} Crystal data are listed in Table 1.

Table 1. Crystallographic data for new compounds.

Compound	3b	4b	4c	5
Formula	C ₆₄ H ₈₀ N ₄ O ₄ S ₂ ·CHCl ₃ ·3C ₂ H ₅ OH	C ₇₀ H ₈₀ N ₄ O ₆ ·2CH ₃ CN·1.5CHCl ₃	C ₆₄ H ₈₀ N ₄ S ₂ O ₆ ·0.5CH ₃ OH·1.5C ₃ H ₆ O	C ₇₂ H ₈₈ N ₄ O ₈ S ₂ ·4CH ₃ CN
Formula weight	1228.30	1334.54	1168.58	1365.80
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	C2/c	P2 ₁ /c	P2 ₁ /c	P-1
a, Å	28.3148(6)	12.6122(5)	19.5803(5)	12.1816(3)
b, Å	15.8506(3)	30.9836(12)	20.1679(5)	24.5969(7)
c, Å	18.2260(4)	18.6901(7)	18.2981(5)	26.7522(7)
α, °	90.00	90.00	90.00	102.923(10)
β, °	118.09(1)	92.349(10)	111.82(3)	95.542(10)
γ, °	90.00	90.00	90.00	98.546(10)
Volume/Å ³	7216.3(3)	7297.4(5)	6708.2(3)	7655.6(4)
Z	4	4	4	4
ρ (calc.), mg/mm ³	1.131	1.215	1.157	1.185
μ, mm ⁻¹	0.181	0.235	0.134	0.129
F(000)	2640	2828	2516	2928
Reflections collected	43374	54294	55928	85996
Independent refl., R _{int}	8708, 0.0464	14329, 0.0926	14623, 0.1568	35131, 0.0544
No. of parameters	420	861	782	1822
Final R _i [I>2σ(I)]	0.0962	0.0852	0.0936	0.0600
wR ₂ (all data)	0.2708	0.2330	0.2441	0.1502
GOF on F ²	1.071	1.004	1.056	1.031

anion binding in this series of disubstituted calixarenes. As a result the compounds exhibit unusual conformational characteristics which offer potential opportunities in anion sensing by conformational switching processes.⁴² Structural characterisation of a range of simple calix[4]arene anion receptors has revealed a finely balanced interplay between intramolecular and intermolecular hydrogen bonding, with intermolecular interactions to the calixarene phenolic oxygen atoms significantly interfering with anion affinity. Increasing the tether length offers a way to decouple the anion binding functionality from the calixarene scaffold, although the consequent increased flexibility must reduce receptor preorganisation.

Experimental

X-ray Crystallography

Suitable single crystals were grown by slow evaporation and mounted using silicon grease on a thin glass fibre. Crystallographic measurements were carried out on a Bruker SMART CCD 6000 and Rigaku R-Axis Spider IP diffractometer using graphite monochromated Mo-Kα radiation

Titration

¹H-NMR titrations were carried out at room temperature using a Varian Inova-500 spectrometer operating at 500 MHz (Durham University). All chemical shifts are reported in ppm relative to TMS as an internal reference. A solution of the host species of known concentration typically 0.5 – 1.5 mM, was made up in an NMR tube using the appropriate deuterated solvent (0.5 ml). Solution of the anions, as TBA salts, were made up in volumetric flasks (2.0 ml) with a concentration five times greater than that of the host. The guest solution was typically added in 10 μl aliquots, representing 0.1 equivalents of the guest with respect to the host. Larger aliquots were used in some cases where no inflection of the trace was evident. Spectra were recorded after each addition and the trace was followed simultaneously. Results were analysed using the curve fitting programme HypNMR.^{31, 32}

Fluorescence spectroscopic titrations were carried out in acetonitrile solution using a PE LS55 Spectrometer at the concentrations stated. See supplementary information.

5,11,17,23-Tetra-*t*-butyl-25,27-bis[[(*N*-*m*-tolylthioureido)oxy]-26,28-dihydroxycalix[4]arene (3b).

5,11,17,23-tetra-*t*-butyl-25,27-bis[(aminoethyl)oxy]-26,28-dihydroxycalix[4]arene²⁴ (0.500 g, 6.80×10^{-4} mol) was reacted with *m*-tolyl isothiocyanate (0.203 g, 1.36×10^{-3} mol) in 25 ml of chloroform. The mixture was stirred for 20 h resulting in the formation of a crude product which was washed 5 ml of hexane, diethyl ether, petroleum ether and propanol to get a pure product.

¹H-NMR (CDCl₃, 700 MHz): 1.10 (18H, s, Bu^t), 1.20 (18H, s, Bu^t), 1.96 (6H, s, CH₃), 3.22 (4H, d, *J* = 14 Hz, ArCH₂Ar), 3.75 (4H, d, *J* = 14 Hz, ArCH₂Ar), 4.08 (4H, m, CH₂), 4.17 (4H, t, *J* = 7 Hz, OCH₂), 6.79 (2H, d, *J* = 7 Hz, Ar), 6.86 (2H, br, NH), 6.90 (4H, s, Ar), 6.92 (4H, s, Ar), 7.03 (2H, t, *J* = 7 Hz, Ar), 7.07 (2H, d, *J* = 7 Hz, Ar), 7.77 (2H, br, NH), 7.93 (2H, t, Ar) and 8.00 (2H, s, OH); ¹³C{¹H}-NMR (CDCl₃, 700 MHz): 21.00 (s, CH₃), 31.09 (s, Bu^t), 31.53 (s, Bu^t), 32.24 (s, ArCH₂Ar), 33.78 (s, ArCH₂Ar), 34.16 (s, CH₂), 46.21 (s, CCH₃), 74.91 (s, OCH₂), 122.91 (s, Ar), 125.47 (s, Ar), 125.96 (s, Ar), 126.38 (s, Ar), 127.75 (s, Ar), 129.00 (s, Ar), 133.11 (s, Ar), 136.31 (s, Ar), 140.02 (s, Ar), 142.57 (s, Ar), 148.03 (s, Ar), 148.29 (s, Ar), 149.29 (s, Ar) and 182.26 (s, CS); Anal. for C₆₄H₈₀N₄O₄S₂·H₂O calc. C 73.10, H 7.67, N 5.32, found C 72.76, H 7.67, N 4.85 %; IR (cm⁻¹) 3283, 2985, 1657, 1484, 1199 and 1034; ESI-MS 1055.5 (C₆₄H₈₀N₄O₄S₂+Na).

5,11,17,23-Tetra-*t*-butyl-25,27-bis[[(*N*-*p*-tolylureido)-ethyl]oxy]-26,28-dihydroxycalix[4]arene (4a).

5,11,17,23-tetra-*t*-butyl-25,27-bis[(aminoethyl)oxy]-26,28-dihydroxycalix[4]arene²⁴ (0.700 g, 9.49×10^{-4} mol) was mixed with *p*-tolyl isocyanate (0.51 g, 3.80×10^{-3} mol) in 50 ml of chloroform solvent. The reaction mixture was refluxed for more than 12h resulting in a formation of crude product, which was washed with slight amount of diethyl ether and hexane solvent to get a pure product.

¹H-NMR (CDCl₃, 400 MHz): 1.15 (18H, s, Bu^t), 1.27 (18H, s, Bu^t), 2.25 (6H, s, CH₃), 3.41 (4H, d, *J* = 12 Hz, ArCH₂Ar), 3.86 (4H, m, CH₂), 4.12 (4H, t, *J* = 8 Hz, OCH₂), 4.19 (4H, d, *J* = 12 Hz, ArCH₂Ar), 6.66 (2H, br, NH), 6.99 (4H, s, Ar), 7.01 (4H, s, Ar), 7.04 (2H, s, Ar), 7.08 (2H, s, Ar), 7.12 (2H, s, Ar), 7.14 (2H, s, Ar), 7.16 (2H, br, NH) and 7.28 (2H, s, OH).

5,11,17,23-Tetra-*t*-butyl-25,27-bis[[(*N*-naphthylureido)-ethyl]oxy]-26, 28- dihydroxycalix[4]arene (4b).

5,11,17,23-tetra-*t*-butyl-25,27-bis[(aminoethyl)oxy]-26,28-dihydroxycalix[4]arene²⁴ (0.200g, 2.72×10^{-4} mol) was mixed with naphthyl isocyanate (0.092 g, 5.44×10^{-3} mol) in 10 ml chloroform solvent at 0 °C. The reaction mixture was stirred for 1h resulting in a formation of crude product and washed with slight amount of diethyl ether, hexane and petroleum ether to get a pure product.

¹H-NMR (Acetone, 700 MHz): 1.03 (18H, s, Bu^t), 1.27 (18H, s, Bu^t), 2.43 (4H, d, *J* = 14 Hz, ArCH₂Ar), 3.87 (4H, m, CH₂), 4.05 (4H, t, OCH₂), 4.25 (4H, d, *J* = 14 Hz, ArCH₂Ar), 7.14 (4H, s, Ar), 7.17 (2H, d, *J* = 7 Hz, Naph), 7.22 (4H, s, Ar), 7.26

(2H, d, *J* = 7 Hz, Naph), 7.30 (2H, br, NH), 7.37 (2H, t, *J* = 7 Hz, Naph), 7.47 (2H, d, *J* = 7 Hz, Naph), 7.75 (2H, d, *J* = 7 Hz, 14 Hz, Naph), 7.84 (2H, m, Naph), 7.93 (2H, brm, Naph), 8.16 (2H, br, NH), and 8.67 (2H, s, OH); ¹³C{¹H}-NMR (Acetone, 700 MHz): 28.70 (s, CH₂), 28.81 (s, Bu^t), 28.92 (s, Bu^t), 29.03 (s, ArCH₂Ar), 29.14 (s, ArCH₂Ar), 76.10 (s, OCH₂), 121.75 (s, Naph), 121.85 (s, Naph), 123.45 (s, Naph), 125.19 (s, Naph), 125.30 (s, Naph), 125.40 (s, Naph), 125.58 (s, Ar), 125.95 (s, Ar), 127.45 (s, Ar), 127.60 (s, Naph), 128 (s, Naph), 142.32 (s, Ar), 147.67 (s, Ar), 149.31 (s, Ar), 150.03 (s, Ar), 150.14 (s, Ar), 156.35 (s, Naph), 156.45 (s, Naph) and 156.54 (s, Naph); Anal. for C₇₀H₈₀O₆N₄·0.2 CHCl₃ calc. C 76.84, H 7.37, N 5.11, found C 77.14, H 7.67, N 4.80; IR (cm⁻¹) 3357, 2960, 1645, 1548, 1483 and 1047; ESI-MS 1072.38 (C₇₀H₈₀O₆N₄-H), 1095.7 (C₇₀H₈₀O₆N₄-H+Na).

5,11,17,23-Tetra-*t*-butyl-25,27-bis[[(*N*-3-methylsulfanyphenylureido)ethyl]oxy]-26,28-dihydroxycalix[4]arene (4c).

5,11,17,23-tetra-*t*-butyl-25,27-bis[(aminobutyl)oxy]-26,28-dihydroxycalix[4]arene²⁴ (0.500g, 6.80×10^{-4} mol) was mixed with 3-methylsulfanyphenyl isocyanate (0.225g, 1.36×10^{-3} mol) in 30 ml of chloroform. The reaction mixture was monitored by TLC while stirring for 4 h. The crude product was washed through slight amount of diethyl ether and hexane solvent to get pure product.

¹H-NMR (Acetone, 700 MHz): 1.05 (18H, s, But), 1.27 (18H, s, But), 2.34 (6H, s, SCH₃), 3.49 (4H, d, *J* = 14 Hz, ArCH₂Ar), 3.93 (4H, m, *J* = 7, 14 Hz, CH₂), 4.07 (4H, t, *J* = 7 Hz, OCH₂), 4.24 (4H, d, *J* = 14 Hz, ArCH₂Ar), 6.80 (2H, d, *J* = 7 Hz, Ar), 6.84 (2H, br, NH), 7.06 (2H, t, *J* = 7, 14 Hz, Ar), 7.11 (2H, d, *J* = 7 Hz, Ar), 7.19 (4H, s, Ar), 7.23 (4H, s, Ar), 7.43 (2H, s, Ar), 8.30 (2H, br, NH) and 8.66 (2H, s, ArOH). ¹³C{¹H}-NMR (Acetone, 700 MHz): 15.28 (s, SCH₃), 30.75 (s, But), 31.37 (s, But), 31.85 (s, ArCH₂Ar), 31.70 (s, ArCH₂Ar), 39.85 (s, CH₂), 76.53 (s, OCH₂), 115.4 (s, Ar), 115.6 (s, Ar), 116.6 (s, Ar), 119.2 (s, Ar), 125.4 (s, Ar), 125.8 (s, Ar), 127 (s, ArOH) and 150 (s, CO); Anal. calc. for C₆₄H₈₀N₄O₆S₂·0.25CHCl₃ C 70.45, H 7.38, N 5.12, found C 70.47, H 7.39, N 5.0 %; IR (cm⁻¹) 3339 (vbr, OH & NH), 2958 (w, CH, str.), 1657 (w, CO), 1537 (s, NH), 1480, 1193; Mass Spectrum ESI 1087.5 (C₆₄H₈₀N₄O₆S₂-H+Na), 1064.3 (C₆₄H₈₀N₄O₆S₂-H).

5,11,17,23-Tetra-*t*-butyl-25,27-bis[[(*N*-dansylureido)-ethyl]oxy]-26,28-dihydroxycalix[4]arene (5).

5,11,17,23-tetra-*t*-butyl-25,27-bis[(aminoethyl)oxy]-26,28-dihydroxycalix[4]arene²⁴ (0.200 g, 2.72×10^{-4} mol) was mixed with dansyl chloride in water and sodium hydrogen carbonate solution (1:1 v/v: 8 ml). The reaction mixture was stirred at room temperature for 2 h resulting in a formation of crude product which was washed with small amount of diethyl ether and hexane to get a pure product.

¹H-NMR (CDCl₃, 700 MHz): 1.12 (18H, s, Bu^t), 1.21 (18H, s, Bu^t), 2.89 (12H, s, NCH₃), 3.01 (4H, m, CH₂), 3.27 (4H, d, *J* = 14 Hz, ArCH₂Ar), 3.81 (4H, t, *J* = 7, OCH₂), 6.98 (4H, s, Ar), 6.99 (4H, s, Ar), 7.11 (2H, m, Naph), 7.29 (4H, m, Naph), 7.49

(2H, d, Naph), 7.50 (2H, br, NH), 7.83 (2H, t, $J = 7$ Hz, Naph), 8.10 (2H, d, $J = 7$ Hz, Naph), 8.39 (2H, d, $J = 7$ Hz, Naph), 8.55 (2H, d, $J = 7$ Hz, Naph) and 8.60 (2H, s, OH); $^{13}\text{C}\{^1\text{H}\}$ -NMR (CDCl_3 , 700 MHz): 30.97 (s, Bu^1), 31.10 (s, Bu^1), 31.45 (s, CH_2), 32.45 (s, CH_2), 42.20 (s, NCH_3), 45.80 (s, CH_2), 76.11 (s, OCH_2), 114.6 (s, Naph), 124 (s, Naph), 125.80 (s, Ar), 126 (s, Ar), 127.8 (s, Naph), 128.5 (s, Naph), 129.80 (s, Naph), 133.50 (s, Ar), 136.31 (s, Naph), 143.04 (s, Ar), 148.18 (s, Naph), 148.50 (s, Ar) and 149 (s, Ar); Anal. for $\text{C}_{72}\text{H}_{88}\text{O}_8\text{S}_2\text{N}_4$ calc. C 71.97, H 7.38, N 4.66, found C 71.77, H 7.37, N 4.69 %; IR (cm^{-1}) 3258, 2954, 2870, 1708, 1462 and 1442; ESI-MS 1224.4 ($\text{C}_{72}\text{H}_{88}\text{O}_8\text{S}_2\text{N}_4 + \text{Na}$).

5,11,17,23-tetra-*t*-butyl-25,27-bis[(*N*-dansylureido)butyl]oxy]-26,28-dihydroxycalix[4]arene (6).

5,11,17,23-tetra-*t*-butyl-25,27-bis[(aminobutyl)oxy]-26,28-dihydroxycalix[4]arene²⁴ (0.724 g, 9.16×10^{-4} mol) was mixed with dansyl chloride in water and sodium hydrogen carbonate solution (1:1 v/v: 8 ml). The reaction mixture was stirred at room temperature for 2.5 h resulting in a formation of crude product which was washed with 3 ml of diethyl ether and hexane to give a pure product.

^1H -NMR (CDCl_3 , 700 MHz): 0.827 (18H, s, Bu^1), 1.24 (18H, s, Bu^1), 1.63 (4H, pt, $J = 6.4$, 13.2 Hz, CH_2), 1.77 (4H, pt, $J = 6.4$, 14, 20 Hz, CH_2), 2.84 (12H, s, NCH_3), 3.180 (4H, m, CH_2), 3.21 (4H, d, $J = 13.2$ Hz, ArCH_2Ar), 3.75 (4H, t, $J = 6.3$, 12.4 Hz, OCH_2), 4.11 (4H, d, $J = 12.8$ Hz, ArCH_2Ar), 6.04 (2H, br, NH), 6.70 (4H, s, Ar), 7.00 (4H, s, Ar), 7.20 (4H, t, $J = 7.6$, 14 Hz, Naph), 7.42 (2H, t, $J = 8$, 16 Hz, Naph), 7.47 (2H, s, OH), 8.22 (2H, d, $J = 7.2$ Hz, Naph), 8.29 (2H, d, $J = 7.2$ Hz, Naph) and 8.46 (2H, d, $J = 8$ Hz, Naph); $^{13}\text{C}\{^1\text{H}\}$ -NMR (CDCl_3 , 700 MHz): 25.70 (s, CH_2), 25.85 (s, CH_2), 30.65 (s, Bu^1), 31.25 (s, Bu^1), 31.60 (s, ArCH_2Ar), 31.80 (s, ArCH_2Ar), 42.28 (s, CH_2), 45.80 (s, NCH_3), 76 (s, OCH_2), 124.59 (s, Ar), 125 (s, Ar), 125.40 (d, Ar), 126 (s, Naph), 126.75 (s, Ar), 128.01 (s, Naph), 128.12 (s, Naph), 129.20 (s, Naph), 129.85 (s, Naph), 131.80 (s, Ar), 148.20 (s, Ar), 148.20 (s, Ar) and 148.90 (s, Ar); Anal. for $\text{C}_{76}\text{H}_{96}\text{O}_8\text{S}_2\text{N}_4$ calc. C 72.58, H 7.69, N 4.45, found C 71.57, H 7.52, N 4.10; IR (cm^{-1}) 3673, 3311, 2953, 1575, 1484, 1311, 1073; ESI-MS 1279.6 ($\text{C}_{76}\text{H}_{96}\text{O}_8\text{S}_2\text{N}_4 + \text{H} + \text{Na}$).

Acknowledgements

We thank Durham University, the Higher Education Commission of Pakistan, Charles Wallace Trust Pakistan and Dr. Wali Muhammad Trust for partial funding.

Notes and references

^a Department of Chemistry, Karakoram International University, Gilgit-Baltistan 15100 Gilgit Pakistan E-Mail: ngq18@hotmail.com.

^b Department of Chemistry, Durham University, South Road, Durham DH1 3LE. E-mail: jon.steed@durham.ac.uk

Electronic Supplementary Information (ESI) available: NMR titration plots, fluorescence spectra and X-ray crystal structures of synthetic intermediates. Crystallographic data have been deposited with the CCDC in CIF format. Deposition numbers CCDC: 1003765-1003769 and 1003934-1003936. See DOI: 10.1039/b000000x/

1. C. D. Gutsche, *Calixarenes Revisited*, Royal Society of Chemistry, Cambridge, 1998.
2. V. Sidorov, F. W. Kotch, G. Abdrakhmanova, R. Mizani, J. C. Fetting and J. T. Davis, *J. Am. Chem. Soc.*, 2002, **124**, 2267-2278.
3. P. Schmitt, P. D. Beer, M. G. B. Drew and P. D. Sheen, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 1840-1842.
4. P. Lhotak, *Top. Curr. Chem.*, 2005, **255**, 65-95.
5. S. E. Matthews and P. D. Beer, *Supramol. Chem.*, 2005, **17**, 411-435.
6. D. B. Qin, X. S. Zeng, Q. S. Li, F. B. Xu, H. B. Song and Z. Z. Zhang, *Chem. Commun.*, 2007, 147-149.
7. J. N. Babu, V. Bhalla, M. Kumar, R. K. Puri and R. K. Mahajan, *New J. Chem.*, 2009, **33**, 675 - 681.
8. F. Sansone, L. Baldini, A. Casnati and R. Ungaro, *New J. Chem.*, 2010, **34**, 2715-2728.
9. O. Hudecek, J. Budka, H. Dvorakova, P. Curinova, I. Cisarova and P. Lhotak, *New J. Chem.*, 2013, **37**, 220-227.
10. J. Scheerder, M. Fochi, J. F. J. Engbersen and D. N. Reinhoudt, *J. Org. Chem.*, 1994, **59**, 7815-7820.
11. E. J. Thomas, S. E. Gabriel, M. Makhlin, S. P. Hardy and M. I. Lethem, *Am. J. Physiol.-Cell Physiol.*, 2000, **279**, C1578-C1586.
12. C. J. E. Haynes and P. A. Gale, *Chem. Commun.*, 2011, **47**, 8203-8209.
13. J. Scheerder, J. F. J. Engbersen, A. Casnati, R. Ungaro and D. N. Reinhoudt, *J. Org. Chem.*, 1995, **60**, 6448-6454.
14. N. A. McDonald, E. M. Duffy and W. L. Jorgensen, *J. Am. Chem. Soc.*, 1998, **120**, 5104-5111.
15. J. Bernstein, R. E. Davis, L. Shimon and N.-L. Chang, *Angew. Chem. Int. Ed. Engl.*, 1995, **34**, 1555-1573.
16. B.-T. Zhao, Y. Liu and H.-Y. Zhang, *J. Mol. Struct.*, 2004, **691**, 25-31.
17. G. Tumchare, T. Tuntulan, S. J. Coles, M. B. Hursthouse and J. D. Kilburn, *Org. Lett.*, 2003, **5**, 4971-4974.
18. E. J. Cho, B. J. Ryu, H. M. Yeo, Y. J. Lee and K. C. Nam, *Bull. Korean Chem. Soc.*, 2005, **26**, 470-472.
19. S. Moerkerke, S. Le Gac, F. Topić, K. Rissanen and I. Jabin, *Eur. J. Org. Chem.*, 2013, **2013**, 5315-5322.
20. D. Cornut, J. Marrot, J. Wouters and I. Jabin, *Org. Biomol. Chem.*, 2011, **9**, 6373-6384.
21. A. Arduini, A. Credi, G. Faimani, C. Massera, A. Pochini, A. Secchi, M. Semeraro, S. Silvi and F. Ugozzoli, *Chem Eur. J.*, 2008, **14**, 98-106.
22. C. D. Gutsche, *Calixarenes*, Royal Society of Chemistry, Cambridge, 1989.
23. C. Baddeley, Z. Yan, G. King, P. M. Woodward and J. D. Badjić, *J. Org. Chem.*, 2007, **72**, 7270-7278.
24. E. M. Collins, M. A. McKervey, E. Madigan, M. B. Moran, M. Owens, G. Ferguson and S. J. Harris, *J. Chem. Soc.-Perkin Trans. 1*, 1991, 3137-3142.
25. J. Scheerder, R. H. Vreekamp, J. F. J. Engbersen, W. Verboom, J. P. M. van Duynhoven and D. N. Reinhoudt, *J. Org. Chem.*, 1996, **61**, 3476-3481.
26. B. R. Cameron and S. J. Loeb, *Chem. Commun.*, 1997, 573-574.
27. M. C. Etter, *Acc. Chem. Res.*, 1990, **23**, 120-126.
28. B. L. Schottel, H. T. Chifotides and K. R. Dunbar, *Chem. Soc. Rev.*, 2008, **37**, 68-83.
29. L. J. Prins, D. N. Reinhoudt and P. Timmerman, *Angew. Chem. Int. Ed.*, 2001, **40**, 2383-2426.
30. V. Bohmer, O. Mogck and W. Vogt, *Tetrahedron*, 1996, **52**, 8489-8496.
31. C. Frassinetti, S. Ghelli, P. Gans, A. Sabatini, M. S. Moruzzi and A. Vacca, *Anal. Biochem.*, 1995, **231**, 374-382.
32. P. Gans, University of Leeds, Leeds, 2006.
33. S. J. Kim, M.-G. Jo, J. Y. Lee and B. H. Kim, *Org. Lett.*, 2004, **6**, 1963-1966.
34. R. Custelcean, *Chem. Commun.*, 2008, 295-307.
35. S. Nishizawa, P. Bühlmann, M. Iwao and Y. Umezawa, *Tetrahedron Lett.*, 1995, **36**, 6483-6486.
36. Y. M. Chung, B. Raman, D.-S. Kim and K. H. Ahn, *Chem. Commun.*, 2006, 186-188.
37. K. R. Dey, B. M. Wong and M. A. Hossain, *Tetrahedron Lett.*, 2010, **51**, 1329-1332.

38. P. Anzenbacher, K. Jursíková and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 9350-9351.
39. G.-Y. Qing, Z.-H. Chen, F. Wang, X. Yang, L.-Z. Meng and Y.-B. He, *Chinese Journal of Chemistry*, 2008, **26**, 721-728.
40. S. R. Holmes-Farley and G. M. Whitesides, *Langmuir*, 1986, **2**, 266-281.
41. Y.-B. Ruan, A. Depauw and I. Leray, *Org. Biomol. Chem.*, 2014.
42. K. J. Wallace, W. J. Belcher, D. R. Turner, K. F. Syed and J. W. Steed, *J. Am. Chem. Soc.*, 2003, **125**, 9699-9715.
43. G. M. Sheldrick, *Acta Crystallogr. Sect. A*, 2008, **64**, 112-122.
44. L. J. Barbour, *J. Supramol. Chem.*, 2001, **1**, 189-191.
45. J. L. Atwood and L. J. Barbour, *Cryst. Growth Des.*, 2003, **3**, 3-8.

Graphical Abstract

The interplay of anion binding, intra- and intermolecular hydrogen bonding patterns in a range of receptors and sensors for chloride anion are discussed.

