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Thermodynamic Characterization of Halide−π Interactions in Solution Using "Two-Wall" Aryl Extended Calix[4]pyrroles as Model System

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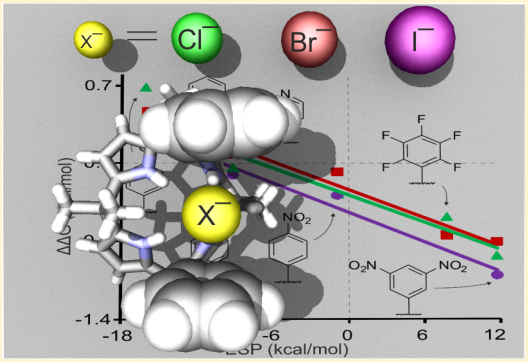
Supporting Information

ABSTRACT: Herein, we report our latest experimental investigations of halide−π interactions in solution. We base this research on the thermodynamic characterization of a series of 1:1 complexes formed between halides (Cl^-, Br^-, and I^-) and several α,α-isomers of "two-wall" calix[4]pyrrole receptors bearing two six-membered aromatic rings in opposed *meso* positions. The installed aromatic systems feature a broad range of electron density as indicated by the calculated values for their electrostatic surface potentials at the center of the rings. We show that a correlation exists between the electronic nature of the aromatic walls and the thermodynamic stability of the X^-⊂receptor complexes. We give evidence for the existence of both repulsive and attractive interactions between π systems and halide anions in solution (between 1 and −1 kcal/mol). We dissect the measured free energies of binding for chloride and bromide with the receptor series into their enthalpic and entropic thermodynamic quantities. In acetonitrile solution, the binding enthalpy values remain almost constant throughout the receptor series, and the differences in free energies are provoked exclusively by changes in the entropic term of the binding processes. Most likely, this unexpected behavior is owed to strong solvation effects that make up important components of the measured magnitudes for the enthalpies and entropies of binding. The use of chloroform, a much less polar solvent, limits the impact of solvation effects revealing the expected existence of a parallel trend between free energies and enthalpies of binding. This result indicates that halide−π interactions in organic solvents are mainly driven by enthalpy. However, the typical paradigm of enthalpy−entropy compensation is still not observed in this less polar solvent.



INTRODUCTION

In 1986, Chowdhury and Kebarle reported gas-phase studies indicating that hexafluorobenzene (C_6F_6), in spite of not having hydrogen atoms binds chloride quite strongly.[1] Thermodynamically stable 1:1 gas-phase adducts with the general formula $[C_6F_6{-}X]^-$ for X^- = Cl^-, Br^-, and I^- could be detected and electronic structure calculations supported the location of the anion above the π-cloud of the aromatic system.[2] In addition, thermochemical data for the gas-phase clustering reactions of the halide ions with C_6F_6 indicated that the bonding strength in the $[C_6F_6{-}X]^-$ complexes derived from electrostatic (Coulombic) interaction. These interesting findings remained dormant in the literature until 2002, when four computational studies reported the existence of general attractive interactions between anions centered over the face of π-systems in six membered cyclic[3−5] and heterocyclic[6] arenes featuring positive quadrupole values. The term "anion−π interaction" was coined to describe this binding motif due to its close structural analogy with the more established noncovalent interaction of cations with π-systems, cation−π interactions.[7]

While attractive cation−π interactions are in tune with chemical intuition, the attractive interaction between an anion and a π system is decidedly contrary to the normal chemist's instinct. Indeed, since their introduction to the greater chemical community in 2002, anion−π interactions have inspired a large number of publications. Numerous and extensive investigations on the physical nature of anion−π interactions and other influencing effects (hydrogen bonds, cations, ring size, etc.) have been performed using electronic structure methods. Anions nestled in the π electron cloud of aromatic rings in single-crystal X-ray structures of supramolecular complexes are frequently highlighted as evidence of attractive anion−π interactions.[8] Several thorough searches of the Cambridge Structural Database (CSD)[3,4,9−11] and Protein Data Bank

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(PDB)[12] have been carried out to demonstrate the existence of anion−π close contacts in archived solid-state structures. However, experimental evidence supporting the existence of attractive anion−π interactions involving charge-neutral aromatic systems in solution is still scarce.[9,13−17] Gas-phase and theoretical studies assign bond energies for supramolecular anion−π interactions in the range of 4−17 kcal mol^{-1}, quite close to those characterizing some cation−π interactions.[18,19] Meanwhile, the values of the stability constants experimentally determined for complexes involving anion−π interactions in solution often do not provide an indisputable assessment of the magnitude of the interaction in this phase.[20−27] So far, this limitation has prevented a confident comparison of the energies that can be assigned to anion−π interactions in solution with respect to their cation−π counterparts. In any case, anion−π interactions have been claimed as a new supramolecular force opening new opportunities for the design of sensors, supramolecular hosts, catalysts, and materials.[28] Functional systems based on anion−π interactions have also been reported.[26,29−33]

We became interested in the experimental study and quantification of anion−π interactions in solution with the aim of increasing the understanding of their physical nature, their magnitude, and their potential applications. The extensive use of benzene panels in shaping the cavity of many molecular and supramolecular containers, i.e., cavitands derived from calix[4]arenes, resocin[4]arenes, and cycloveratrilenes, centered our attention on the quantification of anion−π interactions involving substituted six-membered (phenyl) and charge-neutral rings. In 2008, we designed and synthesized a series of anion receptors based on the $\alpha,\alpha,\alpha,\alpha$-stereoisomer of aryl-extended calix[4]pyrroles **1** bearing four *meso*-phenyl substituents "four-wall" calixpyrroles (Figure 1, left).[34] Different

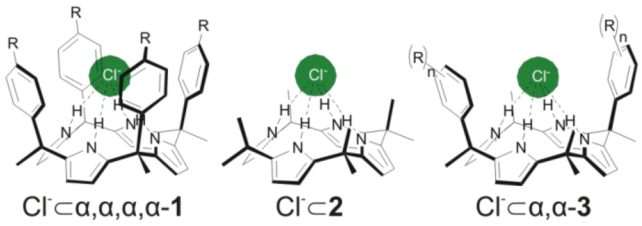

Figure 1. Molecular structures of the inclusion complexes of chloride with "four-wall" aryl extended calixpyrroles **1** (left), "no-wall" octamethylcalix[4]pyrrole **2** (middle), and "two-wall" aryl extended calix[4]pyrroles **3** (right).

para substituents were used to modify the charge density and charge distribution on the surface of the π-system. The extent to which this modification affected the electronics of the aromatic ring was quantified using the corresponding Hammett constants for the *para* substituents. The formation of four hydrogen bonds between the chloride ion and the NH groups of the calix[4]pyrrole unit in **1** induces the receptor to adopt the cone conformation which situates the anion in the deep aromatic cavity paneled by four fixed phenyl walls. The total binding energy, dominated by the strong hydrogen bonding interactions present in the inclusion complexes Cl$^-$⊂**1**, was modulated by the weaker anion−π interactions. Thus, the association constant values determined for the series Cl$^-$⊂**1** increased with the electronic-withdrawing character of the *para* substituent.

This series of "four-wall" calix[4]pyrrole receptors **1** was also used to *quantify* chloride−π(phenyl) interactions in acetonitrile solution. Quantification was achieved by taking the chloride complex of octamethyl calix[4]pyrrole (Cl$^-$⊂**2**) as a reference for the binding energy attributed to the primary hydrogen bonding interaction between the chloride anion and the calix[4]pyrrole core.[35] The difference in binding energy between "four-wall" complexes Cl$^-$⊂**1** and "no-wall" reference Cl$^-$⊂**2** ($\Delta\Delta G$ values) represents the contribution to binding from the interaction between the "four walls" of receptors **1** and the chloride anion. These values correlated well with the corresponding Hammett constants for the *para* substituents. This demonstrated that the observed chloride−π(phenyl) interactions were mainly dominated by electrostatics. In acetonitrile solution, this simple model system allowed us to determine that the interaction between Cl$^-$ and a *p*-NO_2-substituted phenyl group was very slightly attractive; we assigned a magnitude of ca. −0.1 kcal mol^{-1} to this interaction.

In this paper, we report the further study of anion−π interactions in solution using a series of "two-wall" calix[4]-pyrrole receptors **3**. The "two-wall" receptors **3** have several advantages over the "four-wall" analogues. These advantages enable a much more detailed analysis of anion−π interactions. For example, they allow multiple electron-withdrawing substituents to be placed on each of the two *meso*-phenyl walls. In this way, contrary to the original "four-wall" receptors **1**, one can incorporate two *meta* nitro groups or five fluorine atoms around the *meso*-phenyl substituents in **3**. Furthermore, additional *meso*-phenyl substituents were incorporated in receptor series **3**, i.e., pyridyl and *p*-azidophenyl. The availability of these new receptors widens the range of aromatic electrostatic surface potentials (ESP) or quadrupole values that can be interrogated in relation to the energetic magnitude of their interaction with chloride. The deletion of two phenyl *meso* substituents in the "two-wall" receptor series **3** provided an important increase in the thermodynamic stability of the corresponding chloride complexes compared to the their "four-wall" counterparts **1** that feature negative values of ESP at the center of the phenyl rings. This finding was significant as it rendered the series of "two-wall" receptors **3** a suitable model system to investigate the interaction of bromide and iodide with various aromatic rings. These two halides formed complexes with the four walls receptors **1**, deprived of electron-withdrawing groups in their phenyl substituents, which were thermodynamically too weak for the accurate quantification of their binding constants.[36] Finally, in the study presented here we disclose data regarding the enthalpic and entropic components of the anion−π interaction. By dissecting the free binding energy in this way we were able to come to important conclusions regarding dominant factors controlling anion−π interactions and the ability of our model system to analyze and quantify anion−π interactions in solution.

RESULTS AND DISCUSSION

Synthesis and Characterization of the Receptor Series. The synthesis of "two-wall" calix[4]pyrrole receptors α,α-**3** was accomplished using two subsequent acid-mediated condensations (Scheme 1). The first, using pyrrole as the solvent and a methyl phenyl ketone **4**, constructed the aryl-substituted dipyromethane **5**, and the second, using acetone as solvent, effected cyclocondensation to give "two-wall" calix[4]-pyrrole receptors **3**.[37] The methoxy-functionalized receptor α,α-**3a** was obtained through the reaction of the parent

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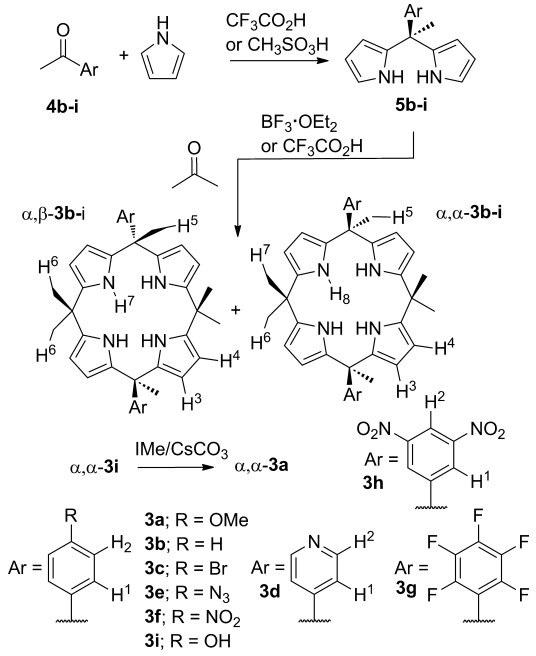
Scheme 1. Synthetic Scheme for the Preparation of the Series of Methylaryldipyromethanes 5b–i and "Two-Wall" Calix[4]pyrroles 3a–i



hydroxyl compound *α,α*-**3i** with methyl iodide in DMF solution using cesium carbonate as base. The syntheses of **3b**,[26] **3e**,[26] **3f**,[38] **3g**,[26] and **3h**[39] have been previously described by our group and others via similar routes.

The ^{1}H NMR spectra of calixpyrroles *α,α*-**3** in CD_3CN solution display two signals for the *β*-pyrrolic protons resonating close to 5.8 ppm ($H^{3\&4}$, Figure 2). The pyrrole NH protons appear downfield shifted at $\delta \approx 8$ ppm, probably due to hydrogen bonding with solvent molecules.

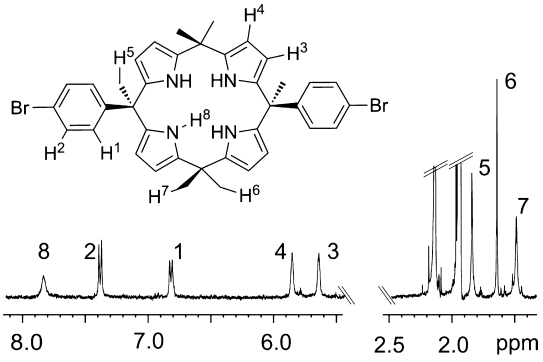


Figure 2. Selected regions of the ^{1}H NMR spectra of two-wall calixpyrrole *α,α*-**3c** in CD_3CN solution at 298 K. The molecular structure indicates proton assignments.

All proton signals are sharp and well resolved. The number of resonances is indicative of either a fast interconversion between conformers (alternate and cone) or a single locked conformation in solution. Thus, consistent with their symmetry, the *α,α*-**3a–h** isomers displayed three signals with the same integral values for the *meso* methyl protons. The structures of several *α,α*-**3** and *α,β*-**3** (see the Supporting Information) calixpyrroles were also confirmed by X-ray crystallography. Single crystals of the *α,α*-**3** isomers grew from dichloromethane, acetonitrile, or acetone solutions revealing that the calix[4]pyrrole core adopted a 1,2 alternate conformation in the solid state (Figure 3).

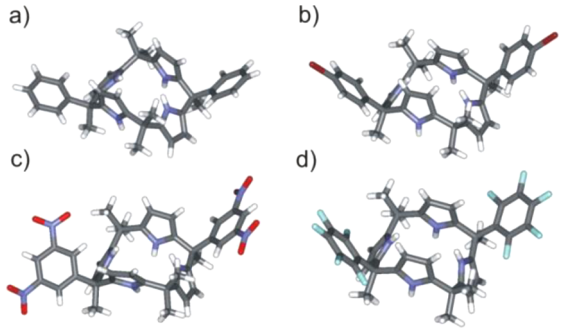


Figure 3. X-ray structures of (a) *α,α*-**3b**, (b) *α,α*-**3c**, (c) *α,α*-**3h**, and d) *α,α*-**3g**. Calix[4]pyrroles all in 1,2 alternate conformation. The *α,α*-**3** calixpyrroles are depicted in stick representation.

^{1}H NMR Titration Experiments with the Halides. Geometries of the Halide Complexes in Solution and in the Solid State. ^{1}H NMR spectroscopy was used to probe the binding of calixpyrroles *α,α*-**3a–h**[40] with chloride in acetonitrile solution.

In particular, ^{1}H NMR was useful in obtaining structural information on the geometry of the complexes and their binding dynamics. We used tetrabutylammonium chloride (TBACl) as the source of the guest chloride anion. In acetonitrile solution and in the range of concentrations used, the tetrabutylammonium salt is highly dissociated and is expected to produce simple anionic 1:1 complexes $Cl^-\subset$*α,α*-**3**.[41]

In a typical example, the initial addition of 0.5 equiv of TBACl to an acetonitrile solution of *α,α*-**3c** (1.1 mM) induced shifting and broadening of most of the proton signals of the receptor (Figure 4).

Exceptions to this general behavior were observed in the titrations of receptors *α,α*-**3h** (3,5-$(NO_2)_2$-Ph) and *α,α*-**3g** (C_6F_5) with chloride. These two receptors contain aromatic walls with multiple, strong electron-withdrawing substituents.

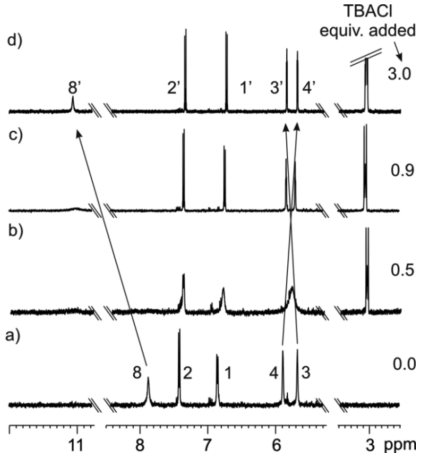


Figure 4. Selected regions of the ^{1}H NMR spectra acquired for the titration of *α,α*-**3c** with TBACl in CD_3CN solution at 298 K. [*α,α*-**3c**] = 1.1 mM. See Figure 2 for proton assignment; primed numbers indicate proton signals for the bound receptor.

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In these two cases, the addition of 0.4 equiv of TBACl induced the appearance of a new set of proton signals alongside the signals belonging to the free receptor. We assigned the new set of signals to protons of the bound receptor in the inclusion complexes $Cl^-\subset\alpha,\alpha$-**3g**&**h**. Separate signals for the fluorine atoms in the free and bound receptor α,α-**3g** were also detected in the ^{19}F NMR spectra (Figure 5).

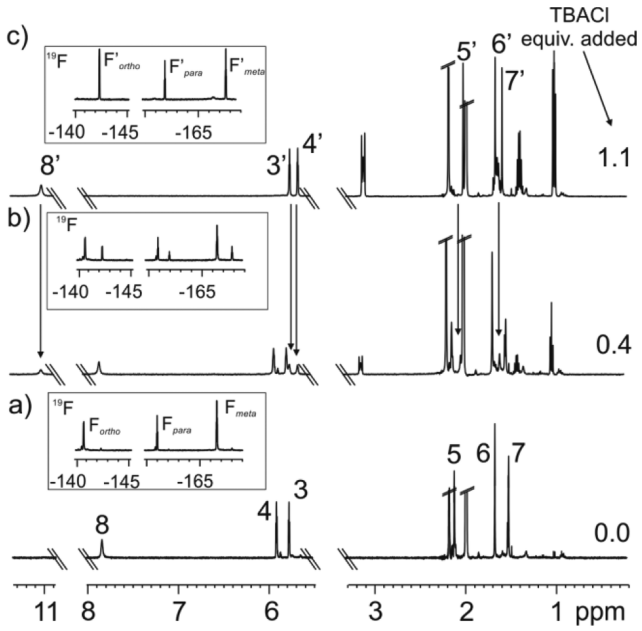

Figure 5. Selected regions of the ^1H NMR spectra acquired for the titration of α,α-**3g** (C_6F_5) with TBACl in CD_3CN solution at 298 K. [α,α-**3g**] = 1.3 mM. The corresponding ^{19}F NMR spectra are depicted as insets. See Scheme 1 for proton assignments; primed symbols indicate proton and fluorine signals for the bound receptor. Arrows are used to allocate this set of proton signals in the slow chemical exchange.

In the ^1H NMR titrations of all receptors α,α-**3a**–**h**, the addition of 1 equiv of TBACl gave rise to the observation of a single set of sharp proton signals corresponding to the receptor in the bound state. The addition of more than 1 equiv of TBACl did not induce additional changes to the proton signals of the receptors. Taken together, the above-described results indicate that the association constant values for the complexes of the receptors α,α-**3a**–**h** binding Cl^- are too high to be measured accurately with ^1H NMR titrations ($>10^4$ M^{-1}) and that receptors α,α-**3h** (di-NO_2) and α,α-**3g** (F_5) form complexes with Cl^- that are kinetically stable on the ^1H NMR time scale.

While NMR spectroscopy was unsuitable for the accurate measurement of binding constants, the technique offered important information about the geometry of the binding complexes $Cl^-\subset\alpha,\alpha$-**3** in acetonitrile solution. Upon chloride binding, the proton signal of the pyrrole NHs (H^8) was shifted significantly downfield ($\Delta\delta$ = 3.00 to 3.23 ppm) while the signals corresponding to the protons of the aromatic walls ($H^{1\&2}$) moved upfield ($\Delta\delta \approx -0.1$ ppm). The downfield shift experienced by the signal belonging to the NHs is consistent with the formation of four hydrogen bonds with the chloride anion. The upfield shift registered for the aromatic protons constitutes clear evidence for the interaction of the chloride ion with the face of the π-system and *not* with the CH groups via CH···Cl^- hydrogen bonds. The upfield shifts observed for the signals corresponding to the fluorine atoms in bound α,α-**3g** (C_6F_5) are also consistent with the existence of chloride–π interactions. No significant changes were detected for the chemical shift values of the proton signals corresponding to the TBA cation. Taking into consideration all the chemical shift changes, we propose the formation of anionic complexes $Cl^-\subset\alpha,\alpha$-**3** in acetonitrile solution featuring a binding geometry in which the calix[4]pyrrole core of the receptor adopts the cone conformation and forms four hydrogen bonds between the pyrrole NHs and the bound chloride. The bound chloride is sandwiched in the cleft defined by the two axially oriented *meso*-phenyl groups (Figure 6, a). This binding geometry is reminiscent of that displayed by the inclusion complexes of chloride with the four-wall analogues $Cl^-\subset\alpha,\alpha,\alpha,\alpha$-**1** (Figure 6, b).[34]

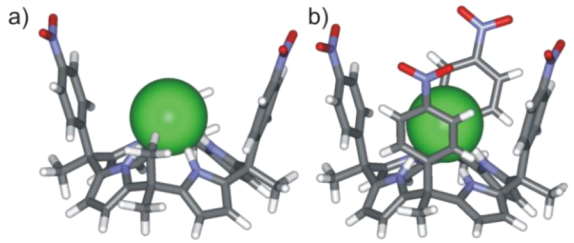

Figure 6. (a) CAChe-minimized structure showing the proposed geometry for the anionic complex $Cl^-\subset\alpha,\alpha$-**3f**; (b) X-ray structure of the analogous four-wall complex $Cl^-\subset\alpha,\alpha,\alpha,\alpha$-**1f**.[34]

It is worth noting that, while the ^1H NMR signal for the β-pyrrole protons of the four wall receptors $\alpha,\alpha,\alpha,\alpha$-**1** moved systematically upfield on chloride binding, the signals for the β-pyrrole protons H^3 and H^4 of the α,α-**3** receptors, with the exception of α,α-**3g**, shifted in opposite directions upon the introduction of chloride. The signal for H^3, located in closer proximity to the phenyl ring than H^4, experienced downfield shifts while the signal for H^4 was upfield shifted. This observation suggests the existence in solution of a conformational change of the calix[4]pyrrole core of the "two wall" receptors α,α-**3**, from alternate to cone conformation upon chloride binding. The solid-state structures are also in support of this hypothesis since, in all cases, they show the free α,α-**3** receptors in the alternate conformation (Figure 3). However, in the inclusion complexes $Cl^-\subset\alpha,\alpha$-**3** the receptors are in cone conformation (Figure 7) vide infra.[42] This is in contrast with the solid state and solution observations for "four-wall" receptors, $\alpha,\alpha,\alpha,\alpha$-**1**, which indicate that the cone conformer is preferred both in the free and bound state.

The formation of anionic complexes $Cl^-\subset\alpha,\alpha$-**3** was also detected by mass spectrometry using electrospray ionization (ESI) and negative detection mode. Receptors α,α-**3** produced anionic complexes with chloride in the gas phase. Using very mild ionization conditions (almost zero voltage), it was possible to detect the peak corresponding to the mass of the $Cl^-\subset\alpha,\alpha$-**3** complexes as the exclusive ion in the 200–1000 m/z range.

As briefly mentioned above, the binding geometry we propose for the inclusion complexes $Cl^-\subset\alpha,\alpha$-**3** in solution is in complete agreement with the structures observed for the corresponding chloride complexes in the solid state. Single crystals of the 1:1 complexes of several α,α-**3** receptors with tetramethylammonium chloride (TMACl) were obtained by slow evaporation of TMACl-saturated acetonitrile or acetone

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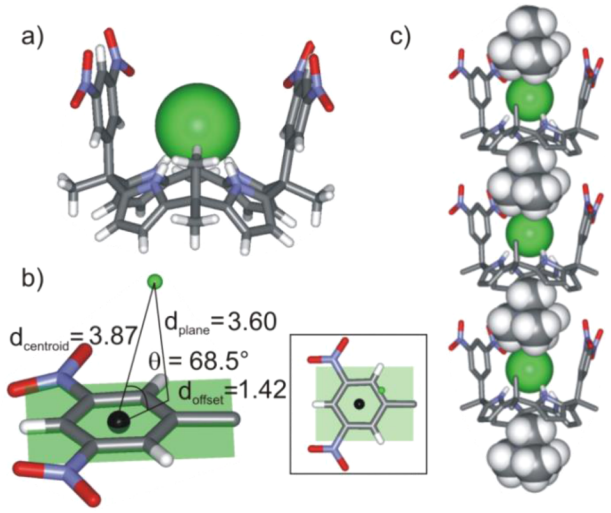

Figure 7. (a) X-ray structure of the $Cl^-\subset\alpha,\alpha$-**3h** complex. (b) Expansion (side and top views) of the region relevant to the chloride-π interaction; important geometrical parameters between the Cl^- and the aromatic ring are indicated. (c) Partial packing of the X-ray structure of TMA·$Cl^-\subset\alpha,\alpha$-**3h**. Distances in angstroms.

solutions of the host. The solid-state structures of the inclusion complexes revealed that the Cl^- atom is not located directly perpendicular to the centroid of the phenyl rings but somewhat offset. The primary hydrogen bonding interactions formed between the Cl^- and the pyrrole NHs ($d_{Cl^-\cdots N} \approx 3.3$ Å) dominate and pull the anion deep inside the aromatic cleft. The geometries of the Cl^-/arene contacts in the complexes are characterized by tilt angles (θ) in the range of 66° to 70° and distances between the mean plane defined by the six carbon atoms of the arene and the Cl^- (d_{plane}) larger than 3.6 Å (3.60–3.99 Å) (see Figure 7).

The observed geometrical parameters of the chloride–π interactions in solid-state structures of the "two wall" complexes are not in ideal agreement with those calculated for chloride–π complexes involving C_6 arenes.[3,4] In the calculated structures, the Cl^- is located above the ring centroid and in close contact with all six arene carbon atoms; that is, all $Cl^-\cdots C$ contacts have a distance < ∑vdw radii (1.70 Å + 1.75 Å = 3.45 Å). This translates to a d_{plane} value <3.16 Å. However, taking into consideration the recent theoretical results described by Estarellas et al.,[43] which indicate that anion–π interactions have less restricted directionality preferences than cation–π interactions and their proposal of the existence of anion–π contacts at distances < ∑wdw radii +0.4 Å = 3.85 Å, the crystal structures of the inclusion complexes $Cl^-\subset\alpha,\alpha$-**3** can be considered as convincing examples of Cl^- interacting with C_6 π systems.

An experimental finding that strongly supports this latter hypothesis is based on the trend observed for d_{plane} in these structures. Generally, this distance decreases as the number and strength of the electron-withdrawing substituents of the ring increase. For example, for the complex $Cl^-\subset\alpha,\alpha$-**3a** (OMe, see Figure S3, Supporting Information) d_{plane} = 3.99 Å. For the complex $Cl^-\subset\alpha,\alpha$-**3h** (3,5-$(NO_2)_2$-Ph, Figure 7) this distance drops to d_{plane} = 3.60 Å.[44] We relate this distance modulation to the strength and character, repulsive or attractive, of the Cl^-–π interactions present in the $Cl^-\subset\alpha,\alpha$-**3** complexes. In short, the geometrical parameters of the Cl^--arene contacts encountered in the solid-state structures of the complexes $Cl^-\subset\alpha,\alpha$-**3** support their use as a model system for the quantification of anion-π interactions in solution. In all solid state structures of the chloride complexes $Cl^-\subset\alpha,\alpha$-**3**, the packing of the crystals revealed that the tetramethyl ammonium cation is in close contact with the bound chloride anion and included into the electronically rich aromatic cavity defined by the pyrrole rings of an adjacent and identical calix[4]pyrrole unit (Figure 7).

The high thermodynamic stability exhibited by the chloride complexes of the "two-wall" receptors α,α-**3** (estimated K_a values higher than 10^4 M^{-1} independently of the electron character of the *meso*-phenyl rings) prompted us to investigate the binding properties of the "two-wall" system with other halides. The complexation of bromide and iodide with receptors α,α-**3b**-**h** was first studied using ^{1}H NMR titrations. The chemical shift changes experienced by the receptor series upon binding bromide or iodide parallel those observed for chloride (Figure S9 (Supporting Information) for I^- and Figure S10 (Supporting Information) for Br^-). The most notable difference in the binding behavior with the larger halides was the magnitude of the complexation-induced shift experienced by the ^{1}H NMR signal corresponding to the pyrrole NHs. As the halide radii increased, the difference between the free and bound chemical shift values of the NH protons decreased. Thus, the change in chemical shift for the NH protons binding bromide is $\Delta\delta \approx 2.5$ ppm and only $\Delta\delta \approx 1.9$ ppm for iodide, compared to $\Delta\delta$ = 3.0 to 3.2 ppm for chloride.[45] This behavior is anticipated given the expected trend in hydrogen bond strength between different halides and the calix[4]pyrroles **3** (I^- weaker than Br^- weaker than Cl^-).

Single crystals suitable for X-ray analysis grew from acetonitrile solutions of receptor α,α-**3g** (F_5) saturated with tetramethylammonium chloride, bromide, and iodide salts. The X-ray structures revealed the formation of inclusion complexes TMA·$X^-\subset\alpha,\alpha$-**3g** with structural features similar to those described above (Figure 8).The comparison of the crystal structures of the inclusion complexes of the three halides with the same receptor TMA·$X^-\subset\alpha,\alpha$-**3g** exposed several similarities and differences. The general binding geometry of the 1:1 complexes and the conformation adopted by the receptor is almost identical independently of the included anion. The distance between the centroids of the C_6F_5 aromatic rings is maintained more or less constant throughout the series of complexes ($d_{centroids} \approx 7.9$ Å).This result demonstrated that the inclusion of the bigger iodide anion is not sterically hindered.

The increase in radius of the anion is also responsible for the observed change in distance between the centroid defined by the four N atoms of the pyrrole rings and the center of the halide. In turn, this difference in the placement of the halide translates to a modification of the tilt angle θ that characterizes the position of the anion with respect to the center of the aromatic C_6F_5 ring. For the TMA·$I^-\subset\alpha,\alpha$-**3g** complex the geometry of the iodide–π interaction is very close to that predicted by theory, having the I^- in contact with five of the ring carbons to within ∑vdW + 0.4 Å and a tilt angle of $\theta \approx$ 80°. Taken together, these results show that in the solid state, bromide, iodide and chloride behave similarly in the way that they bind two-wall calix[4]pyrrole receptors α,α-**3** and that the receptor series constitutes a valuable and valid model system for the quantification of halide–π interactions in solution.

Using ^{1}H NMR spectroscopy (receptor concentration ≈1 mM), "two-wall" receptors lacking electron-withdrawing substituents on their *meso*-phenyl walls α,α-**3a** (OMe) and α,α-**3b** (H) did not show detectable interactions with iodide.[46]

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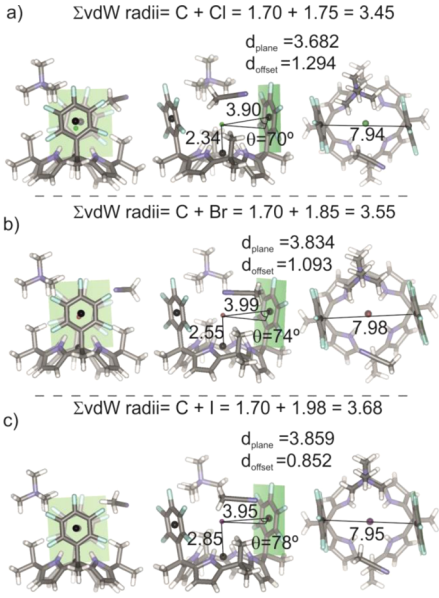

Figure 8. Front, side, and top views of the X-ray structures of 1:1 inclusion complexes of receptor *α,α*-**3g** with tetramethylammonium halide salts: (a) Cl^-, (b) Br^-, and (c) I^-. Selected geometrical parameters for one of the two anion−*π* contacts are indicated. The black dots represent calculated centroids. The structures are shown with all atoms in stick representation. Using the criteria introduced in ref 43 for the existence of anion−*π* contacts, the crystal structures of the three inclusion complexes X^-⊂*α,α*-**3g** can be considered as convincing examples of X^- interacting with C_6 *π* systems. Distances in angstroms.

However, ^{1}H NMR spectroscopic titrations of the examples comprised of more electron-poor walls proved to be suitable for the determination of binding constants. Thus, using this technique, we obtained binding data for the interaction of iodide with receptors *α,α*-**3d,f,g,h**. ^{1}H NMR spectroscopic titration was also a viable technique to determine the binding constants for some of the "two wall" calixpyrrole receptors with bromide. The thermodynamic data obtained in the ^{1}H NMR titration experiments are summarized in Table 1. However, similarly to their interaction with chloride, receptors *α,α*-**3g** and *α,α*-**3h** containing the most electron-poor aromatic walls showed binding with bromide that was too strong to be accurately measured by NMR spectroscopy.

Isothermal Titration Calorimetry Experiments. Thermodynamic Characterization of the Inclusion Complexes X^-⊂*α,α*-3 and the Halide−*π* Interaction. For the accurate determination of the binding constant values that were estimated to be higher than 10^4 M^{-1} from the results of ^{1}H NMR titration experiments, we relied on isothermal titration calorimetry (ITC) experiments.[47,48] An ITC experiment affords, in a single run, information on the enthalpy and entropy of the interaction, complex stoichiometry, and association constant values. All the ITC experiments performed with the *α,α*-**3** receptor series and chloride showed excellent fits to the theoretical binding isotherm for a 1:1 complex formation. We include in Figure 9 two representative examples

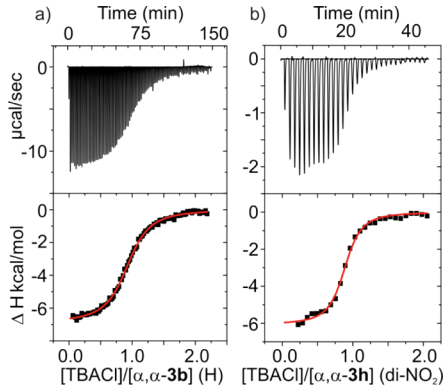

Figure 9. (Top) Raw data (heat vs time) for the ITC titrations of (a) *α,α*-**3b** (*R* = H) and (b) *α,α*-**3h** (di-NO_2) receptors with TBACl. (Bottom) Normalized integration of heat vs Cl^-/*α,α*-**3** molar ratio; the fit of the 1:1 theoretical binding isotherm (red line) to the experimental data is also shown. The values returned in the fitting procedure for all ITC experiments are summarized in Tables 1 and 2. [*α,α*-**3b**] = 1.3 mM and [*α,α*-**3h**] = 0.1 mM.

Table 1. Association Constant Values (K_a, M^{-1}) and Free Energies of Complexation (Δ*G*, kcal/mol) Measured in MeCN at 298 K for the Inclusion Complexes of the Three Halide Anions with the Receptor Series *α,α*-3 and the Reference Octamethyl Calix[4]pyrrole 2, and Statistically Corrected Free Energy Values Calculated for the Anion−*π* Interactions (ΔΔ*G*, kcal/mol)[a]

		halide								
		chloride			bromide			iodide		
receptor	ESP[b]	$K_a \times 10^{-3}$	Δ*G*	ΔΔ*G*[e]	$K_a \times 10^{-3}$	Δ*G*	ΔΔ*G*[e]	K_a	Δ*G*	ΔΔ*G*[e]
2(Me)	n/a	108[d]	−6.9	n/a	3.6[d]	−4.9	n/a	12.6[c]	−1.5	n/a
3a(OMe)	−16.1	10.6[d]	−5.5	0.7						
3b(H)	−15.9	26.5[d]	−6.0	0.4	0.8[c]	−3.9	0.5			
3c(Br)	−9.7	67.8[d]	−6.6	0.1	2.8[c]	−4.7	0.1			
3d(Py)	−9.2	124[d]	−6.9	0.0	2.3[d]	−4.6	0.1	18.2[c]	−1.7	−0.1
3e(N_3)	−8.9	60.1[d]	−6.5	0.2	1.4[c]	−4.3	0.3			
3f(NO_2)	−0.9	277[d]	−7.4	−0.3	4.7[d]	−5.0	−0.1	33.5[c]	−2.1	−0.3
3g(C_6F_5)	7.7	553[d]	−7.8	−0.5	32.3[d]	−6.2	−0.6	*f*		
3h(di-NO_2)	11.8	1790[d]	−8.5	−0.8	39.5[d]	−6.3	−0.7	380[c]	−3.5	−1.0

[a]ITC titration experiments were repeated at least twice, and the reported K_a is the mean of the values obtained from the fit of the integrated heat data to a 1:1 binding model. NMR titration experiments were also repeated at least twice, and the reported K_a is the mean of the values obtained from the fit of the chemical shift changes observed for the proton signals to a 1:1 binding model. Errors for Δ*G* are assumed to be in the region of ±20%. [b]Value of the electrostatic surface potential at the center of the aromatic ring. [c]Determined by NMR spectroscopic titration. [d]Determined by ITC. [e]$\Delta\Delta G = (\Delta G_{X^-\subset 3} - \Delta G_{X^-\subset 2})/2$. [f]Data from the titration of *α,α*-**3g** with TBAI failed to fit well to a 1:1 model (see the Supporting Information for details).

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of ITC experiments. The association constant values for all $Cl^-\subset\alpha,\alpha$-**3** inclusion complexes and the bromide inclusion complexes with octamethyl calix[4]pyrrole **2** (Me), α,α-**3e** (Py), α,α-**3f** (NO_2), α,α-**3g** (F_5), and α,α-**3h** (di-NO_2) were determined using ITC experiments.

As alluded to above, in acetonitrile solution, and at the concentration range used for the ITC titrations, both the salt used as the source for the chloride/bromide/iodide anion ($TBA^+\cdot X^-$) and the resulting complex ($X^-\subset\alpha,\alpha$-**3**$\cdot TBA^+$) are considered to be fully dissociated.[41,49,50] This is evidenced by the fact that the halide-binding constants measured for TMA and TBA salts are the same. Thus, the equation we used for the calculation of the stability constants of the 1:1 complexes formed by receptors α,α-**3** and halide anions (X^- = Cl^-, Br^-, I^-) in acetonitrile solution is as follows and has units of M^{-1}.

$$K_a = \frac{[X^-\subset\alpha,\alpha\text{-}\mathbf{3}]}{[X^-][\alpha,\alpha\text{-}\mathbf{3}]} \quad (1)$$

Association constant values K_a and the derived Gibbs free energies (ΔG) for the 1:1 inclusion complexes of the α,α-**3** receptor series with chloride, bromide, and iodide anions in acetonitrile at 298 K are listed in Table 1. For a given α,α-**3** receptor, the stability constant value determined for the iodide complex is predictably smaller than that with bromide which, in turn, is predictably smaller than that with chloride. This observation supports the importance of electrostatics (mainly hydrogen bonds) in the overall binding affinity of the receptor series for the halides. The influence of the type of halide on the energetics of the anion–π interaction will be discussed below.

Traditionally, Hammett plots have been used to rationalize and quantify electrostatic trends in experimental data. We and others[51] have noticed that the Hammett constants of *meta*-substituents attached to aromatic rings, σ_m, show a linear correlation with the electrostatic surface potential (ESP) values calculated at the center of those aromatic rings. Similar plots using B3LYP/6-31G* level calculations show that the same trend exists for Hammett constants of *para*-substituents, σ_p. In the work presented here, there is a mixture of *para* monosubstitution and *meta*-disubstitution of phenyl rings, in addition to the pentafluorophenyl and pyridyl groups. To better describe this diverse range of aromatic systems, we calculated the ESP values at the center of the ring in lieu of using the Hammett constants. In this way, we simply generated a scale that expresses the electronic properties of the surfaces above the *meso*-aromatic rings employed in this study.[52] The values of the calculated ESPs at the center of each *meso*-aromatic group are listed in Table 1 and become more positive going through the series of receptors from α,α-**3a** to α,α-**3h**.

We have mentioned above that the main interaction in the stabilization of the $X^-\subset\alpha,\alpha$-**3** complexes is the formation of hydrogen bonds between the halide and the pyrrole NHs of the receptor. Throughout the receptor series α,α-**3**, we observed a close similarity in the values of the chemical shift of the free pyrrole NH protons. Likewise, the complexation induced shift experienced by the NHs upon halide binding is very similar and is only a function of the halide type. Furthermore, calculations of EPN values at the pyrrole nitrogen nuclei of representative dipyromethanes point to similar pK_a values for the pyrrole NH groups across the series of receptors α,α-**3a** to α,α-**3h** and reference system **2**.[53] These observations suggest that, for a given anion, it is sensible to consider that the strength of the principal hydrogen bonding interaction remains constant throughout the series $X^-\subset\alpha,\alpha$-**3** and $X^-\subset$**2**. This claim is also supported by the solid state structures of the $Cl^-\subset\alpha,\alpha$-**3** complexes where it can be clearly seen that the distances between the pyrrole nitrogen and the chloride remain constant throughout the receptor series.

Thus, we considered the values of the free energies of binding for the complexes $X^-\subset\alpha,\alpha$-**3** as the sum of two different and independent types of intermolecular interaction: (a) hydrogen bonding and (b) anion–π interaction. On the basis of this hypothesis and for any one of the investigated halides, the differences in the free energies of binding calculated between any two of the complexes $X^-\subset\alpha,\alpha$-**3** provide a direct measurement of the relative interaction energy of the anion with the different *meso*-aromatic π-systems.

The free energies of binding determined for the complexes of "no-wall" octamethyl calix[4]pyrrole with the different halides $X^-\subset$**2** constitute suitable references of the contribution solely from hydrogen bonding to the binding of halides with the receptor series α,α-**3**. By subtracting this value from the free energy of binding for the same halide with a "two-wall" calix[4]pyrrole α,α-**3** (eq 2) we calculated the contribution to total binding from the anion–π interactions. This value was then statistically corrected (divided by two) to calculate the value of the anion–π interaction between the halide and one of the various *meso*-aromatic systems in the complexes $X^-\subset\alpha,\alpha$-**3** (Table 1).

$$\Delta\Delta G = \frac{\Delta G(X^-\subset \mathbf{3}) - \Delta G(X^-\subset \mathbf{2})}{2} \quad (2)$$

In this calculation, we assume that the anion–π interactions are additive. That is, there is little to no effect caused by one anion–π interaction on the other. Such an assumption seems reasonable given theoretical studies on the interactions of halides with triazine rings, which suggest that anion–π interactions are indeed additive.[54]

For the three halides, the determined $\Delta\Delta G$ values correlate well with the ESP values calculated at the centroid of the respective aromatic walls (Figure 10).[55]

A likely explanation to the observed trend is consistent with anion–π interactions being governed by electrostatics. The

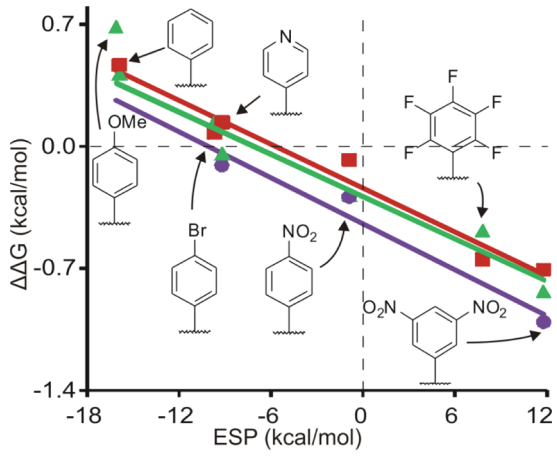

Figure 10. Plot of the experimental values for the anion-π interaction derived from the binding of chloride (green ▲), bromide (red ■), or iodide (purple ●) with two-wall calix[4]pyrroles α,α-**3** correlate with the ESP values calculated at the centroid of the aromatic walls. For clarity, data for calixpyrrole α,α-**3e** is not shown. See the Supporting Information for a complete plot.

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slopes of the correlation lines for each halide are very similar.[56] While the existence of electrostatic interactions also serves to explain why bromide owing to the increase in its atomic radius binds slightly weaker than chloride, they do not account for the noticeably more favorable interactions measured for iodide, about 0.2 kcal mol^{-1} more favorable. It looks as though describing the interaction as purely electrostatic and dependent on the ESP value at the ring's center is reasonable but perhaps slightly too simplistic. In fact, a plain electrostatic anion−π interaction should favor the chloride anion due to its higher charge density and reduced size. The increased size and polarizability of the iodide anion with respect to the other halides is likely the reason for its stronger anion−π interactions. We speculate that the induction of dipoles is maximized in the case of iodide due to its larger volume and reduced electronegativity. Most likely, the electrostatic attraction in the iodide−π complexes is enhanced by the high polarizability of the iodide, resulting in additional Debye−Hückel attractions between the partial positive charge on the aromatic surface and the induced dipole of the anion or vice versa through partial charge transfer. van der Waals interactions are also maximized for I^- since the surface contact in the idoide−π complexes is larger. Finally, the geometry of the I^-−π contact observed in the solid state for the complex $I^-\subset\alpha,\alpha$-**3g** (Figure 8, c) closely resembles that theoretically predicted as the energy minimum for anion−π interactions involving a C_6 aromatic ring.

The anion−π interactions between the electron-rich surfaces of the phenoxy and phenyl groups (α,α-**3a** and α,α-**3b**, respectively) and chloride, bromide and iodide (in the latter case extrapolated from the corresponding regression line) are all faintly repulsive (∼0.3−0.7 kcal mol^{-1}). Then, as the ESP values of the aromatic systems become increasingly positive, the halide−π interactions become attractive. Eventually, the interactions of all halides with the very π-acidic C_6F_5 and (3,5-$(NO_2)_2$-Ph) systems (α,α-**3g** and α,α-**3h** respectively) are noticeably attractive (∼ −0.7 to −1.0 kcal/mol).

As discussed above, the binding of chloride with all receptors α,α-**3a**−**h** and the binding of bromide with the more electron poor receptors α,α-**3d** and α,α-**3f**−**h** was investigated by ITC. Thus, it was possible to dissect the free energies of binding into their enthalpic (ΔH) and entropic ($T\Delta S$) components (Table 2 and Figure 15).

As expected for binding processes taking place in a nonprotic organic solvent and dominated by the formation of hydrogen bonds, all events were mainly enthalpically driven and highly exothermic. Also, as expected for complexation processes relying on electrostatic forces (hydrogen bonds and anion−π interactions), the binding of receptors α,α-**3** with chloride (−5.8 to −7.6 kcal/mol) was more exothermic than with bromide (−4.2 to −5.1 kcal/mol). However, quite surprisingly for us, the magnitude of the enthalpies of binding for a common halide remained relatively constant across the series of receptors α,α-**3** or even displayed a slightly inverted trend with respect to the free energies of binding (Figure 11, lower). Indeed, the binding of chloride to the most electron-rich calixpyrroles α,α-**3a** and α,α-**3b** is actually slightly more enthalpically favorable than the binding of chloride with the most electron poor examples α,α-**3g** and α,α-**3h**. A similar trend was seen for the binding of bromide.[57] Clearly, the almost constant value of the enthalpic term (ΔH) for halide binding across the series of calixpyrroles α,α-**3** does not parallel the trend seen for the free energies of binding (ΔG) and consequently neither for the free energy values ascribed to the halide-π interactions ($\Delta\Delta G$).

Table 2. Experimental Values for the Enthalpic (ΔH, kcal/mol) and Entropic ($T\Delta S$, kcal/mol, 298 K) Components of the Free Energy of Binding for the Complexes of Chloride and Bromide with "Two-Wall" Calix[4]pyrroles α,α-3 in Acetonitrile Solution[a]

		chloride		bromide	
receptor	ESP	ΔH	$T\Delta S$	ΔH	$T\Delta S$
2	n/a	−8.7	−1.6	−5.7	−0.9
3a(OMe)	−16.1	−6.9	−0.8		
3b(H)	−15.9	−6.1	−0.6		
3c(Br)	−9.7	−6.2	0.3		
3d(py)	−9.2	−6.2	0.8	−5.1	−0.5
3e(N_3)	−8.9	−6.2	0.3		
3g(NO_2)	−0.9	−6.2	−1.2	−5.0	0
3h(F_5)	7.7	−6.4	1.4	−4.8	1.3
3i(di-NO_2)	11.8	−5.8	2.7	−4.2	2.1

[a]The values presented are the mean of those obtained from at least two ITC titration experiments. Errors for ΔH and $T\Delta S$ are assumed to be in the region of ±20%.

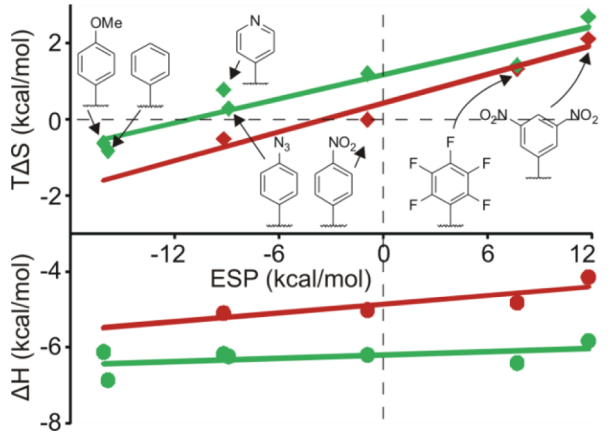

Figure 11. Plot of the experimental values for the enthalpic (lower, circles, ΔH, kcal/mol) and entropic (upper, diamonds, $T\Delta S$ at 298 K, kcal/mol) components of the free energy of binding for the complexes of chloride (green) or bromide (burgandy) with two-wall calix[4]-pyrroles α,α-**3** plotted against the ESP values at the center of the respective *meso*-aromatic rings. For clarity, data for calixpyrrole α,α-**3c** is not shown. See the Supporting Information for a complete plot.

At first sight, these results may be considered as a rare example of a binding process showing a linear free energy relationship that is not a consequence of an enthalpy−entropy compensation effect.[58,59] We are accustomed to relate an increase in stability (ΔG) for a series of related 1:1 complexes formed in nonprotic organic solvents to a gain in enthalpy (stronger binding) resulting in a more organized complex (loss of entropy, weaker binding). Such a scenario will correspond to the most common enthalpy−entropy compensation effect. We rationalized that the unexpected trends observed here for the thermodynamic quantities ΔH and $T\Delta S$ are blurred by solvation effects that occur during the binding process. On the one hand, both the magnitudes and the trend of the free energy values determined for the series of complexes correlate well with our simplistic picture of a 1:1 binding process in the gas phase, where energetically more favorable anion-π interactions should lead to thermodynamically more stable

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complexes. On the other hand, the dissection of Gibbs energies into their enthalpic and entropic terms highlights the shortcomings associated with the interpretation of these magnitudes using the same simplistic physical model of a 1:1 complex formation that fails to consider solvation effects.

During the binding process, many of the constrained acetonitrile molecules involved in solvating the receptor and the anion will be released to the bulk solution. This will result in two important effects. First, if the molecules released to the bulk solvent form less strong interactions between themselves than when solvating the halide and the receptor, this will be accompanied by a loss of enthalpy. This means that the measured enthalpy for the binding process is actually the combination of the enthalpies of host–guest binding and solvent reorganization ($\Delta H_{obs} = \Delta H_{X^-\subset 3} + \Delta H_{solvation}$), both terms being complex dependent. Second, the desolvation of host and guest is typically characterized by a gain in entropy owing to the release of several solvent molecules to the bulk solution. Conversely, the formation of the 1:1 complex occurs under loss of translational and rotational entropy of one of the two components and may also restrict the conformational motion of the host. The sum of these terms provides the overall entropy value for the inclusion process in solution and explains why a gain in entropy can be observed experimentally. We must conclude that, in general, solvation effects render the physical interpretation of the enthalpic and entropic components of free energies of binding very complicated.

Due to the unexpected thermodynamic behavior seen in our system, we performed binding experiments in other solvents. Not surprisingly, analysis of chloride binding in acetone revealed a very similar situation to that seen in acetonitrile (see Table S2 and Figures S4 and S21 in the Supporting Information). In particular, we looked to move the system into a nonpolar solvent that would minimize solvation effects and better approximate the gas phase host–guest complexation. In order to do so, we turned from the tetrabutylammonium (TBA) chloride salt, which due to ion pairing and lack of cation-receptor size complementarity shows only weak interactions in nonpolar solvents like chloroform,[60] to the methyl trioctylammonium chloride salt (MTOACl). Methyltrialkyl ammonium chloride salts are known to form receptor-separated ion paired complexes with calix[4]pyrroles in chlorinated solvents.[61] Contrary to the above-described binding experiments carried out in acetonitrile solution where bimolecular anionic complexes $X^-\subset\alpha,\alpha$-**3** were formed, the binding of MTOACl in chloroform yields trimolecular neutral ion-paired complexes $Cl^-\subset$**3**·MTOA. Despite this significant difference, in chloroform solution, inclusion complexes between MTOACl and "two-wall" calixpyrroles display the same binding geometry regarding the anion and the aryl-extended calixpyrrole core.[62] In other words, the complex $Cl^-\subset$**3**·MTOA will still place the anion in the aromatic cleft, sandwiched between the two phenyl *meso*-substituents and interacting with their π systems. Furthermore, if one considers that in chloroform, MTOACl is highly ion-paired, as well as the resulting complex $Cl^-\subset$**3**·MTOA, then, as in acetonitrile, the binding event can be considered as the formation of a 1:1 complex, exhibiting an association constant reported in units of M^{-1} (eqs 3 and 4).

$$\alpha,\alpha\text{-}\mathbf{3} + \text{MTOACl} \rightleftarrows \text{Cl}\subset\alpha,\alpha\text{-}\mathbf{3}\cdot\text{MTOA} \quad (3)$$

$$K_a = \frac{[\text{Cl}\subset\alpha,\alpha\text{-}\mathbf{3}\cdot\text{MTOA}]}{[\text{MTOACl}][\alpha,\alpha\text{-}\mathbf{3}]} \quad (4)$$

Thus, the differences in stability constants for the complexes formed between the calix[4]pyrrole receptor series α,α-**3b**-–**h** and MTOACl in chloroform can be directly ascribed to the different binding affinities for chloride. This can be done because only the anion-binding site is significantly modified. In this way, the binding data obtained for the receptor series and MTOACl in chloroform (see eq 4) can be related to that obtained with TBACl in acetonitrile (see eq 1). In accordance with this hypothesis, across the receptor series, the values obtained for the free energies of the Cl^--π interaction ($\Delta\Delta G$) in chloroform with MTOACl matched very well with those observed in acetonitrile with TBACl (Table S3 and Figure S6, Supporting Information). Conversely, ΔH and $T\Delta S$ for the complexes between MTOACl and the receptor series α,α-**3b**-**h** in chloroform painted a different picture to that seen in acetonitrile with TBACl[63] (Table S2 (Supporting Information), and Figure 12, chloroform results in blue and acetonitrile results in green).

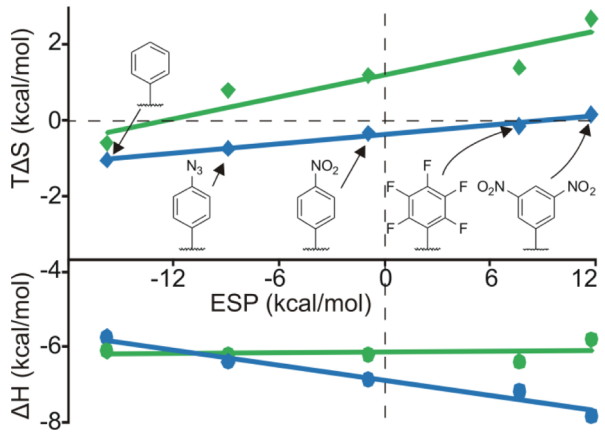

Figure 12. Plot of the experimental values for the enthalpic (lower, circles, ΔH, kcal/mol) and entropic (upper, diamonds, $T\Delta S$ at 298 K, kcal/mol) components of the free energy of binding for the complexes of TBACl in acetonitrile (green) or MTOACl in chloroform (blue) with two-wall calix[4]pyrroles α,α-**3** plotted against the ESP values at the center of the respective *meso*-aromatic rings.

In chloroform, the slope of the line defined by the entropic quantities ($T\Delta S$) across the receptor series is still positive but is much less pronounced than in acetonitrile. The entropy values are slightly negative or very close to zero. Significantly, in the less polar solvent the enthalpic component of binding (ΔH) is still highly exothermic but becomes more negative (attractive) going from Cl$\subset\alpha,\alpha$-**3b**·MTOA to Cl$\subset\alpha,\alpha$-**3h**·MTOA. These results strongly suggest that, as expected, anion–π interactions are mainly enthalpic in nature and that the unexpected enthalpic and entropic quantities observed in acetonitrile are due to solvation effects. Our findings also serve as a caveat for the direct interpretation of the enthalpic and entropic magnitudes of binding processes where major changes in solvation of host and/or guest are experienced upon complex formation.

CONCLUSION

In conclusion, we have characterized thermodynamically the binding of chloride, bromide, and iodide with a variety of two-

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wall calix[4]pyrrole receptors α,α-**3**. The receptor series α,α-**3** exhibits a variety of electronically different aromatic walls. While bound to the calix[4]pyrroles, the anions are wedged in the cleft formed by the two aromatic walls and sandwiched between them. The anions are, therefore, forced to interact, either repulsively or attractively, with the corresponding π systems. Halide binding becomes progressively more attractive as the number and electron withdrawing character of the aromatic substituents increases (more positive ESP value at the center of the six member ring). This may be considered as evidence for the presence of anion-π interactions and the electrostatic nature of those interactions. Comparison of binding energies for the "two-wall "system α,α-**3** with binding energies for the "no-wall" reference calix[4]pyrrole **2** allows a rough quantification of the strengths of the various halide-π interactions. Chloride and bromide experience interactions with π systems that are very similar in strength and reach attractive magnitudes of up to −0.7 kcal mol^{-1}. Iodide experiences slightly more attractive interactions with π systems, up to −1.0 kcal mol^{-1}, a phenomenon that we ascribe to the increased size and polarizablility of iodide in relation to the other halides.

The binding processes were analyzed more thoroughly via their enthalpic and entropic terms. Unexpectedly, in acetonitrile solution, the increase in free energy of binding (ΔG) of halides with receptors having aromatic rings with the more positive ESP values, correlates with a more positive entropic contribution ($T\Delta S$) to binding. In addition, the free energies values and their enthalpic contributions (ΔH) show a subtle inverted trend. We ascribed this unexpected behavior to strong solvation effects taking place during the binding process. Indeed, upon changing to a less polar solvent, chloroform, the binding data displayed the expected relationship of free energy and enthalpy of binding in nonpolar organic solvents, by which an increase in free energy is reflected by an increase in binding enthalpy. However, even in chloroform solution the model system under study does not obey the common enthalpy−entropy compensation paradigm. We suggest that the loss of entropy leading to complex formation is compensated by a significant gain in entropy accompanying the almost complete desolvation of the ion-pair. This desolvation is required for the formation of receptor-separated ion-paired $Cl^-\subset\alpha,\alpha$-**3**·TOA complexes. Finally, our results indicate that anion−π interactions in polar and nonpolar organic solvents can be weakly attractive −0.7 to −1 kcal mol^{-1} and that they are mainly driven by enthalpy.[64]

■ ASSOCIATED CONTENT

Supporting Information

General experimental methods for the synthesis and binding studies, fits of the titration data, additional experimental results discussed in the text and their associated figures, spectral data for new compounds, and X-ray crystallographic files of **5c**, **5d**, **5h**, α,α-**3a**, α,α-**3b**, α,α-**3c**, α,α-**3g**, α,α-**3h**, α,β-**3c**, α,β-**3g**, and α,β-**3h** and the inclusion complexes TMACl$\subset\alpha,\alpha$-**3a**, TMACl$\subset\alpha,\alpha$-**3b**, TMACl$\subset\alpha,\alpha$-**3c**, TMACl$\subset\alpha,\alpha$-**3g**, TMACl$\subset\alpha,\alpha$-**3h**, TBABr$\subset\alpha,\alpha$-**3f**, TMABr$\subset\alpha,\alpha$-**3g**, TMABr$\subset\alpha,\alpha$-**3h**, and TMAI$\subset\alpha,\alpha$-**3g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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