Calix[4]pyrroles with bulky substituents and their anion binding studies

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Abstract: Calix[4]pyrrole derivatives with bulky substituents at their meso-positions were synthesized via mixed condensation of pyrrole with cyclohexanone and acetophenone derivatives. Anion binding studies, carried out by isothermal titration calorimetry in 1,2-dichloroethane with Cl\(^{-}\) and CH\(_3\)CO\(_2\) anions in the form of their tetrabutylammonium salts, revealed that these new calix[4]pyrrole derivatives can bind the aforementioned anions as effectively as the unsubstituted “parent” system, octamethylcalix[4]pyrrole (1). Structural characterizations of new calix[4]pyrroles were carried out by using \(^1\)H and \(^{13}\)C NMR spectroscopy corroborated with mass spectrometry.

Key words: Calix[4]pyrrole, anions sensors, anion binding

1. Introduction

Anions play crucial roles in environmental chemistry,\(^1,2\) biological processes,\(^3\) biomedicine,\(^4-6\) and regulation of human health.\(^7\) Their particular importance in the agricultural industry\(^8\) and nuclear fuel cycle\(^9\) makes anions and their recognition chemistry particularly important. This significance led scientists to investigate the chemistry of anions and their interactions with selective anion receptors.\(^10,11\) Within this realm, selective optical sensors, phase transfer catalysts, and chromatographic stationary phases have been prepared and used for the determination and separation of different anionic species.\(^12\) However, the weak nature of the anion-receptor interactions, reflecting the relatively low charge density of most anions, prompted researchers to design sophisticated anion receptor systems to achieve better control of recognition and selectivity.

While many reported anion receptors have proven to be quite effective,\(^13,14\) calix[4]pyrroles (1 and 2 in Figure 1) have become some of the anion receptors that are easiest to make.\(^15,16\) This is because the core and functional structures can be accessed in one synthetic step and a large number of modifications are readily conceivable.\(^17,18\) The first calix[4]pyrrole compound, octamethylcalix[4]pyrrole (1), was synthesized by Baeyer in 1886 via a condensation reaction of pyrrole and acetone in the presence of an acid catalyst.\(^19\) Conformation change from 1,3-alternate to cone was discovered by Sessler and coworkers in 1996. In that study, anion-calix[4]pyrrole complexes were formed via hydrogen bonding between pyrrole NHs and target anions. The distances between the nitrogen and the anion were in the range of 3.264–3.331 Å.\(^15\) After the discovery of their anion recognition ability, various calix[4]pyrrole derivatives were prepared by a number of research groups to improve the binding affinity and tune the sensing capability of these macrocycles. These valuable studies include expanded,\(^20\) N-confused,\(^21,22\) C-rim modified\(^23\) chromophore and fluorophore modified,\(^24-27\) functionalized

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nanoparticles,\textsuperscript{28–30} and redox active calix[4]pyrrole derivatives.\textsuperscript{31,32} In addition to proven ion-pair recognition ability,\textsuperscript{18,33} well-defined oligomers\textsuperscript{34} and polymers\textsuperscript{35–38} of calix[4]pyrroles have also been reported and it was shown that these macrocyclic anion receptors can be used for the extraction of F\textsuperscript{−} and Cl\textsuperscript{−} anions, in the form of their tetrabutylammonium salts, from aqueous solutions. Moreover, enhanced extraction of KF and KCl from aqueous solutions has also been shown when the crown ether moieties were incorporated into the polymer matrix along with calix[4]pyrrole receptor sites.\textsuperscript{36} These intriguing findings prompted us to develop new highly organic soluble calix[4]pyrrole compounds for further potential use in the removal of anionic species from aqueous environments.

\begin{center}
\includegraphics[width=\textwidth]{figure1}
\end{center}

\textbf{Figure 1.} Structures of octamethylcalix[4]pyrrole and tetraspirocyclohexylcalix[4]pyrrole.

In this study, in the context of our synthetic efforts, cyclic aliphatic and aromatic units were incorporated into the macrocyclic structure of the calix[4]pyrrole core to maintain high solubility in organic solvents while keeping the selectivity of the macrocycle against different anionic species. Therefore, we focused on the synthesis and characterization of a new set of calix[4]pyrroles and investigated the anion binding properties of these compounds using isothermal titration calorimetry (ITC).

The present study was motivated by a desire to obtain calix[4]pyrroles that would not partition significantly into water when studied under potential interfacial conditions. Recently we demonstrated that the attachment of long \(n\)-alkyl ester units to the calix[4]pyrrole core structure can help maintain high solubility in organic solvents.\textsuperscript{39} This is because certain calix[4]pyrroles could be used to reverse the so-called Hofmeister bias\textsuperscript{33,40} and are thus potentially useful as anion extractants. Anion extraction is an application of minimizing surface water eutrophication originating from agricultural runoff\textsuperscript{8} and a function of the nuclear waste processing industry.\textsuperscript{9} As another step towards these long-term goals, we sought to develop new calix[4]pyrroles prepared from cyclohexanone and acetophenone derivatives. These new calix[4]pyrroles could prove to be soluble in common organic solvents and could preserve the selective recognition of specific anionic species.

\section*{2. Results and discussion}

\subsection*{2.1. Synthesis and characterization}

To prepare the target calix[4]pyrrole derivatives and compare their anion binding affinities we followed two different pathways. The first strategy was the preparation of 4-phenyl substituted tetraspirocyclohexyl calix[4]pyrrole compounds (Scheme 1). The presence of a large number of aliphatic carbon atoms and phenyl units was expected to provide highly organic soluble calix[4]pyrroles. Therefore, we carried out a number of mixed condensation
reactions of pyrrole with 4-phenylcyclohexanone and cyclohexanone in methanol using methanesulfonic acid as a catalyst. These reactions afforded compounds 3 and 4 in 86% and 45% yields, respectively.

$^1$H and $^{13}$C NMR spectroscopy data corroborated with the mass analyses proved the consistency of the products with the expected structures. Phenyl units connected to cyclohexyl rings were anticipated result in four possible configurational isomers ($\alpha\alpha\alpha\alpha$, $\alpha\alpha\alpha\beta$, $\alpha\beta\alpha\beta$, $\alpha\alpha\beta\beta$)\textsuperscript{41,42} of compound 3 and two similar isomers ($\alpha\alpha$, $\alpha\beta$) for 4 based on the relative orientations of the phenyl units. Although we were not able to separate these isomers using conventional chromatographic techniques, the presence of the configurational isomers is not expected to change the anion binding strength of either 3 or 4 dramatically since the phenyl units are far enough away from the macrocycle cores.

The presence of configurational isomers was observed in the $^1$H NMR spectra of compounds 3 and 4. For instance, the pyrrole –CH proton resonances were observed as two distinctive multiplet peaks at 5.80 and 5.93 ppm for 3 (Figure 2). In the case of compound 4 pyrrole CH resonance multiplets were observed between 5.85 and 6.17 ppm. These results are consistent with the expected configurational isomers of 3 and 4. Similarly, the aromatic protons of phenyl units also gave rise to multiplet resonance signals between 7.00 and 7.14 ppm for both of 3 and 4. Additionally, distinctive NH resonances at 6.87 and 7.30 ppm for calix[4]pyrrole 3 and at 7.07 and 7.21 ppm for the calix[4]pyrrole 4 are consistent with the structures of these compounds.

In the second strategy we used cyclohexanone and acetophenone derivatives to obtain new calix[4]pyrrole compounds as shown in Scheme 2. Phenyl units connected to the meso-positions of calix[4]pyrroles are known to increase the anion binding affinity of these structures via anion $\pi$ interactions.\textsuperscript{43} Furthermore, the presence of cyclohexyl units at the meso-positions was expected to increase the solubility of the calix[4]pyrroles in common organic solvents. Thus, incorporation of the phenyl and cyclohexyl derivatives was expected to increase the anion binding affinity of the calix[4]pyrroles via additional anion $\pi$ interactions while maintaining the high solubility in organic solvents. This would also allow us to compare the effect of phenyl units and substituents at their 4-positions on the anion binding abilities when compared with the parent systems (1 and 2). With these aims, compounds 5 and 6 were prepared using conditions similar to those used to prepare 4 to afford 5 and 6 in 49% and 52% yields, respectively (Scheme 2). These compounds were also characterized by using $^1$H and $^{13}$C NMR spectroscopy and mass spectrometry. The presence of phenyl units at the meso-positions of 5 and 6 was expected to result in the formation of two possible configurational isomers ($\alpha\alpha$ and $\beta\beta$) based on the relative orientations of phenyl units when the calix[4]pyrrole core was considered as a plane.\textsuperscript{41,42} Accordingly, two distinctive multiplet resonance signals belonging to the pyrrole –CH protons between 5.69 and 5.93 ppm were attributed to the configurational isomers of 5 and 6. Pyrrole NH resonances at 7.01 and 7.51 ppm for
compound 5 and at 7.15 and 7.20 ppm for macrocycle 6 are also consistent with the integrity of the structures. Configurational isomers of 5 and 6 were inseparable during column chromatography and were used as a mixture for further analyses.


The third strategy was using 4-phenylcyclohexanone and acetophenone derivatives to compare the effect of extra phenyl units attached to the cyclohexanone ring. For that purpose, 4-chloro and 4-iodo derivatives of acetophenone were used to prepare mixed condensation products. Compounds 7, 8, and 9 were obtained in 45%, 42%, and 40% yields, respectively, as illustrated in Scheme 2. Characterization of these compounds was accomplished by the same techniques used for the other calix[4]pyrrole derivatives of this study. Similar to above set of calix[4]pyrroles, these compounds were also expected to have configurational isomers. Relative orientations of phenyl units attached to both meso-positions of the calix[4]pyrrole core and the cyclohexyl rings resulted in the formation of these inseparable isomers. The presence of isomers was confirmed by $^1$H NMR analysis. For instance, two distinctive multiplet pyrrole –CH resonance signals at 5.83 and 5.92 ppm and at 5.80 and 6.10 ppm raised by calix[4]pyrroles 7 and 8, respectively, reflected the presence of configurational isomers. Compound 9 showed relatively sharper pyrrole –NH peaks at 5.80 and 6.10 ppm. These proton signals as well as the pyrrole –NH resonances were consistent with the expected structures of compounds 7–9.

![Scheme 2. Synthesis of calix[4]pyrrole derivatives 5–9.](image)
2.2. Anion binding studies

Anion binding measurements of compounds 3–9 were carried out in 1,2-dichloroethane. This relatively apolar solvent was chosen because the binding measurements of 1 and our previous set of calix[4]pyrrole compounds were carried out in 1,2-dichloroethane. Thus, ready reference to these benchmark data could be made and, with this goal in mind, the chloride and acetate binding properties of calix[4]pyrroles 3–9 were analyzed in 1,2-dichloroethane at room temperature using ITC (See Supplementary Materials for ITC titration curves).

The Table shows the binding constants for the calix[4]pyrroles of this study interacting with Cl\(^-\) and CH\(_3\)CO\(_2\)^- in the form of their tetrabutylammonium salts. Compound 5, the mixed condensation product of cyclohexanone and acetophenone, shows similar affinity to 1 towards chloride anion. This suggested to us that the presence of cyclohexyl units would help the calix[4]pyrrole core structure to take the cone conformation as easily as 1 when it is bound to an anion. A similar trend was observed in the case of compound 6, which is the mixed condensation product of cyclohexanone and 4-iodoacetophenone. This result corroborates the conformational effect of cyclohexyl units connected to the meso-position of the calix[4]pyrrole ring. Interestingly, calix[4]pyrrole 7, which was obtained by the mixed condensation of 4-phenylcyclohexanone and acetophenone, showed better anion binding affinity. Compound 7 binds the chloride anion about three times more strongly than parent system 1 and more effectively than compounds 5 and 6. Similarly, compound 9 binds the chloride anion more strongly than the aforementioned compounds. These results suggested that the phenyl units at meso-positions and connected to 4-positions of the cyclohexyl units enhance the chloride anion binding constants, presumably because of the additional anion–π interactions. The major conclusion supported by the chloride binding data in the Table is that the presence of phenyl units in the meso-positions of the calix[4]pyrrole ring increases the anion binding affinity by a factor of 2–3 depending on the substituents on the phenyl units of acetophenone. The affinity constants for compounds, 3, 4, and 8 could not be determined because of competing but as of yet identified interactions observed in the ITC traces.

**Table.** Chloride and acetate anion binding affinities (1/M) measured in 1,2-dichloroethane (as the tetrabutylammonium salt) using ITC. Estimated errors are less than 10%.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cl(^-)</th>
<th>CH(_3)CO(_2)^-</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.8 x 10(^{14})</td>
<td>4.4 x 10(^{14})</td>
</tr>
<tr>
<td>3</td>
<td>n.d.</td>
<td>6.0 x 10(^4)</td>
</tr>
<tr>
<td>4</td>
<td>n.d.</td>
<td>6.6 x 10(^4)</td>
</tr>
<tr>
<td>5</td>
<td>1.0 x 10(^4)</td>
<td>6.5 x 10(^4)</td>
</tr>
<tr>
<td>6</td>
<td>1.5 x 10(^4)</td>
<td>2.3 x 10(^4)</td>
</tr>
<tr>
<td>7</td>
<td>9.7 x 10(^3)</td>
<td>1.3 x 10(^4)</td>
</tr>
<tr>
<td>8</td>
<td>n.d.</td>
<td>1.8 x 10(^4)</td>
</tr>
<tr>
<td>9</td>
<td>4.9 x 10(^3)</td>
<td>2.7 x 10(^4)</td>
</tr>
</tbody>
</table>

*a*Taken from reference (42). *b*Taken from reference (39). *c*n.d.: not determined.

Enhanced acetate anion binding affinity was observed compared to octamethylcalix[4]pyrrole 1 in the case of compound 3 possessing four phenyl units that are on the 4-positions of cyclohexyl units. The same trend was not observed in the case of compound 4. The acetate anion binding affinity of compound 4 containing two phenyl units on the 4-positions of the cyclohexyl units is ten times less than that of compound 3. This may be because compound 4 possesses only two 4-phenyl cyclohexyl units. A similar trend was also observed in the case of compound 5. Furthermore, replacing the 4-phenylcyclohexyl units with the cyclohexyl units increases the acetate anion binding affinity that was observed with compounds 7, 8, and 9. For example, compound 7
binds acetate twice as much as 5. It can finally be concluded that all the calix[4]pyrrole compounds of this work having phenyl units on the 4-positions of the cyclohexyl components show better acetate anion binding affinities compared to the corresponding calixpyrroles containing cyclohexyl units.

3. Experimental

3.1. Materials and measurements

Melting points were measured on a Gallenkamp instrument and are uncorrected. $^1$H and $^{13}$C NMR spectra used in the characterization of products were recorded on a Bruker 250 MHz AC-3000 spectrometer. Low-resolution FAB and CI mass spectra were obtained on a Finningan MAT TSQ 70 mass spectrometer. High-resolution FAB and CI mass spectra were obtained on a VG ZAB2-E mass spectrometer. The ESI-MS data were recorded on a Waters/Micromass ZQ mass spectrometer. Microcalorimetric titrations were performed using an isothermal titration calorimeter purchased from MicroCal Inc. (USA). The experimental temperature was 25 °C. The ORIGIN software provided by MicroCal Inc. was used to calculate the binding constants ($K_a$) and the enthalpy change ($\Delta H$). The solvent, C$_2$H$_4$Cl$_2$, was of HPLC grade but was not further dried or purified before use. Tetrabutylammonium chloride and tetrabutylammonium acetate were dried under vacuum at 40 °C for 24 h before use. All solvents were dried before use according to standard literature procedures. Unless specifically indicated, all other chemicals and reagents used in this study were purchased from commercial sources and used as received.


Pyrrole (1 mL, 14.3 mmol) and 4-phenylcyclohexanone (1.49 mL, 14.3 mmol) were dissolved in MeOH (100 mL) at 0 °C and bubbled with N$_2$ for 15 min. Following this bubbling, methanesulfonic acid (650 µL, 10 mmol) was then added drop-wise to the mixture over the course of 30 min while shielding the reaction vessel from light. The resulting mixture was then stirred first at 0 °C for 3 h and subsequently at room temperature for 15 h. The white precipitate that formed during this time was collected by filtration and washed with MeOH to get rid of the soluble impurities. Chromatographic purification (silica gel, dichloromethane/hexanes: 1/1, v/v) afforded 3 as a white solid (2.78 g, 86%). Mp: decomposes over 210 °C; $^1$H NMR (250 MHz, CDCl$_3$) δ (ppm) = 1.67 (br m, 16H, CH$_2$), 1.88 (br m, 8H, CH$_2$), 2.28 (br m, 8H, CH$_2$), 2.60 (br, 4H, CH), 5.81–6.19 (m, 8H, pyrrole-CH), 6.87 (2H, NH), 6.97–7.14 (br m, 20H, phenyl CH), 7.30 (2H, NH). $^{13}$C NMR (60 MHz, CDCl$_3$): δ (ppm) = 147.23, 139.93, 139.22, 138.45, 133.75, 128.34, 126.74, 125.96, 107.31, 106.49, 105.80, 102.48, 101.71, 100.33, 43.98, 39.46, 38.04, 37.54, 36.48, 30.65 ppm. LRMS (ESI): 892 ([M$^+$]). HRMS (ESI): 893.5517 ([M$^+$]$, C_{64}$H$_{69}$N$_4$; calc. 893.5545).


Pyrrole (1 mL, 14.3 mmol), cyclohexanone (0.75 mL, 7.15 mmol), and 4-phenylcyclohexanone (1.25 g, 7.15 mmol) were dissolved in MeOH (100 mL) at 0 °C and bubbled with N$_2$ for 15 min. Following this bubbling, methanesulfonic acid (650 µL, 10 mmol) was then added dropwise to the mixture over the course of 30 min while shielding the reaction vessel from light. The resulting mixture was then stirred first at 0 °C for 3 h and subsequently at room temperature for 15 h. The white precipitate that formed during this time was collected by filtration and washed with MeOH to get rid of the soluble impurities. Chromatographic purification (silica gel, dichloromethane/hexanes: 4/1, v/v) yielded 4 as a white solid (1.20 g, 45%). Mp: 182–184 °C; $^1$H NMR
(250 MHz, CDCl$_3$) $\delta$ (ppm) = 1.56 (12H, CH$_2$), 1.76 (br m, 12H, CH$_2$), 2.05 (br t, 8H, $J = 6.2$ Hz, CH$_2$), 2.26 (br d, 4H, $J = 7.4$ Hz, CH$_2$), 2.59 (br t, 2H, $J = 6.1$ Hz, CH), 5.85–6.17 (br m, 8H, pyrrole CH), 7.03 (2H, NH), 7.07–7.21 (br m, 10H, phenyl CH), 7.36 (2H, NH). $^{13}$C NMR (60 MHz, CDCl$_3$) $\delta$ (ppm) = 147.24, 138.82, 138.46, 133.22, 128.33, 126.75, 125.95, 107.77, 106.76, 105.82, 102.22, 101.23, 43.97, 37.38, 30.59, 26.03, 22.79. LRMS (ESI): 740 ([M$^{-}$]). HRMS (ESI): 741.4899 ([M+H$^+$], C$_{52}$H$_{61}$N$_4$; calc. 741.4896).


This compound was prepared from pyrrole (1 mL, 14.3 mmol), cyclohexanone (0.75 mL, 7.15 mmol), and acetophenone (0.84 mL, 7.15 mmol) using a procedure analogous to that used to prepare 4. The product was a white solid (1.11 g, 49%). Mp: 154–156 °C; $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ (ppm) = 1.51 (br m, 12H, CH$_2$), 1.87 (s, 6H, CH$_3$), 1.95 (br m, 8H, CH$_2$), 5.69 (m, 4H, pyrrole CH), 5.93 (m, 4H, pyrrole CH), 7.01 (2H, NH), 7.20–7.25 ppm (m, 10H, phenyl CH), 7.51 (2H, NH, pyrrole CH). $^{13}$C NMR (60 MHz, CDCl$_3$) $\delta$ (ppm) = 148.12, 137.89, 136.73, 135.94, 135.35, 127.43, 126.31, 106.34, 105.85, 104.11, 103.26, 44.64, 39.70, 38.74, 37.42, 35.74, 28.18, 25.98, 22.76. LRMS (ESI): ([M+H$^+$]) 633; HRMS (ESI): 633.3952 ([M+H$^+$], C$_{44}$H$_{49}$N$_4$I$_2$; calc. 633.3978).


This compound was prepared from pyrrole (1 mL, 14.3 mmol), cyclohexanone (0.75 mL, 7.15 mmol), and 4-iodoacetophenone (1.77 g, 7.15 mmol) using a procedure analogous to that used to prepare 4. The product was a yellow solid (1.65 g, 52%). Mp: decomposes over 155 °C; $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ (ppm) = 1.48 (br m, 12H, CH$_2$), 1.84 (s, 6H, CH$_3$), 1.95 (br m, 8H, CH$_2$), 5.78 (4H, pyrrole CH), 5.92 (4H, pyrrole-CH), 6.76 (d, $J = 6.8$, 2H, phenyl CH), 6.85 (d, $J = 6.8$, 2H, phenyl CH), 7.15 (2H, NH), 7.20 (2H, NH), 7.56 (m, 4H, phenyl CH). $^{13}$C NMR (60 MHz, CDCl$_3$) $\delta$ (ppm) = 22.74, 25.96, 27.87, 35.36, 37.38, 39.89, 44.51, 91.98, 103.92, 106.10, 129.57, 135.09, 136.31, 136.86, 137.42, 146.89, 147.92. LRMS (ESI): ([M+H$^+$]) 885. HRMS (ESI): 885.1885 ([M+H$^+$], C$_{44}$H$_{47}$N$_4$I$_2$; calc. 885.1868).


This compound was prepared from pyrrole (1 mL, 14.3 mmol), 4-phenylcyclohexanone (1.26 g, 7.15 mmol), and acetophenone (0.84 mL, 7.15 mmol) using a procedure analogous to that used to prepare 4. The product was a yellow solid (1.27 g, 45%). Mp: 150–152 °C; $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ (ppm) = 1.84–1.96 (br m, 14H, CH$_2$ and CH$_3$), 2.31 (br m, 8H, CH$_2$), 2.64 (br m, 2H, CH), 5.83 (4H, pyrrole CH), 5.92 (4H, pyrrole CH), 7.01 (2H, NH), 7.18–7.29 (m, 20H, phenyl CH), 7.45 (2H, NH). $^{13}$C NMR (60 MHz, CDCl$_3$) $\delta$ (ppm) = 23.48, 25.77, 28.98, 34.43, 38.63, 39.45, 46.81, 93.12, 104.52, 108.74, 131.47, 134.92, 139.56, 140.24, 145.94, 148.41. LRMS (ESI MS): ([M+H$^+$]) 785. HRMS (ESI MS): 785.4578 ([M+H$^+$], C$_{56}$H$_{57}$N$_4$; calc. 785.4605).


This compound was prepared from pyrrole (1 mL, 14.3 mmol), 4-phenylcyclohexanone (1.26 g, 7.15 mmol), and 4-chloroacetophenone (1.11 g, 7.15 mmol) using a procedure analogous to that used to prepare 4. The product was a brownish solid (1.30 g, 42%). Mp: 168–170 °C; $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ (ppm) = 1.48 (br m, 4H, CH$_2$), 1.86 (br m, 14H, CH$_2$ and CH$_3$), 2.29 (br m, 4H, CH$_2$), 2.62 (br m, 2H, CH), 5.81 (4H, pyrrole
CH), 5.95 (4H, pyrrole CH), 6.98 (2H, NH), 7.15-7.27 (br m, 20H, phenyl CH and NH). $^{13}$C NMR (60 MHz, CDCl$_3$): 30.28, 37.29, 37.86, 39.04, 39.38, 43.97, 101.27, 126.02, 126.70, 127.76, 128.32, 128.82, 132.19, 133.24, 140.51, 147.05 ppm. LRMS (FAB MS): ([M + H$^+$]) 853; HRMS (FAB MS): 853.3798 ([M+H$^+$], C$_{56}$H$_{55}$N$_4$Cl$_2$; calc. 853.3795).


This compound was prepared from pyrrole (1 mL, 14.3 mmol), 4-phenylcyclohexanone (1.26 g, 7.15 mmol), and 4-iodoacetophenone (1.77 g, 7.15 mmol) using a procedure analogous to that used to prepare 4. The product was a brownish solid (1.50 g, 40%). Mp: decomposes over 160 $^\circ$C; $^1$H NMR (250 MHz, CDCl$_3$): 1.52 (br s, 4H, CH$_2$), 1.85 (br m, 14H, CH$_2$ and CH$_3$), 2.23 (br m, 4H, CH$_2$), 2.63 (br m, 2H, CH), 5.80 (4H, pyrrole CH), 6.10 (4H, pyrrole CH), 6.73 (2H, NH), 6.82 (m, 4H, phenyl CH), 7.17 (br m, 12H, phenyl CH and NH), 7.58 (m, 4H, phenyl CH). $^{13}$C NMR (60 MHz, CDCl$_3$) ppm = 22.64, 30.19, 30.44, 37.41, 39.40, 43.86, 44.55, 91.95, 126.03, 126.74, 128.36, 129.59, 133.33, 136.97, 139.68, 140.52, 147.08. LRMS (CI): ([M + H$^+$]) 1037; HRMS (ESI): ([M+H$^+$]) 1037.2520, C$_{56}$H$_{55}$N$_4$I$_2$; calc. 1037.2516.

Acknowledgement

Special thanks to Professor Jonathan L Sessler (The University of Texas at Austin, USA) for providing the ITC instrument for anion binding studies.

References

Supplementary Materials

1. ITC titration studies

Microcalorimetric titrations were performed using an isothermal titration calorimeter (ITC) purchased from MicroCal Inc. (USA). The experimental temperature was 25 °C. The ORIGIN software provided by MicroCal Inc. was used to calculate the binding constants ($K_a$) and the enthalpy change ($\Delta H$). The solvent, $C_2H_4Cl_2$, was of HPLC grade (Fisher) but was not further dried or purified before use.

2. ITC titration for compound 3

![Figure S1](image)

**Figure S1.** ITC titration curves obtained from the titration of compound 3 (0.4 mM) with acetate anion (8 mM) in $C_2H_4Cl_2$ at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.
3. ITC titration for compound 4

![ITC titration curve](image1)

**Figure S2.** ITC titration curves obtained from the titration of compound 4 (0.4 mM) with acetate anion (6 mM) in 
C\textsubscript{2}H\textsubscript{4}Cl\textsubscript{2} at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.

4. ITC titration for compound 5

![ITC titration curve](image2)

**Figure S3.** ITC titration curves obtained from the titration of compound 5 (0.4 mM) with chloride anion (6 mM) in 
C\textsubscript{2}H\textsubscript{4}Cl\textsubscript{2} at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.
5. ITC titration for compound 5

![ITC titration for compound 5](image)

Figure S4. ITC titration curves obtained from the titration of compound 5 (0.4 mM) with acetate anion (8 mM) in C$_2$H$_4$Cl$_2$ at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.

6. ITC titration for compound 6

![ITC titration for compound 6](image)

Figure S5. ITC titration curves obtained from the titration of compound 6 (0.4 mM) with chloride anion (6 mM) in C$_2$H$_4$Cl$_2$ at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.
7. ITC titration for compound 6

![ITC titration curve for compound 6](image)

**Figure S6.** ITC titration curves obtained from the titration of compound 6 (0.4 mM) with acetate anion (8 mM) in C$_2$H$_4$Cl$_2$ at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.

8. ITC titration for compound 7

![ITC titration curve for compound 7](image)

**Figure S7.** ITC titration curves obtained from the titration of compound 7 (0.4 mM) with chloride anion (6 mM) in C$_2$H$_4$Cl$_2$ at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.
9. ITC titration for compound 7

Figure S8. ITC titration curves obtained from the titration of compound 7 (0.4 mM) with acetate anion (8 mM) in C₂H₄Cl₂ at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.

10. ITC titration for compound 8

Figure S9. ITC titration curves obtained from the titration of compound 8 (0.4 mM) with acetate anion (6 mM) in C₂H₄Cl₂ at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.
11. ITC titration for compound 9

![ITC titration curve for compound 9 with chloride anion](image)

**Figure S10.** ITC titration curves obtained from the titration of compound 9 (0.4 mM) with chloride anion (8 mM) in C₂H₄Cl₂ at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.

12. ITC titration for compound 9

![ITC titration curve for compound 9 with acetate anion](image)

**Figure S11.** ITC titration curves obtained from the titration of compound 9 (0.4 mM) with acetate anion (6 mM) in C₂H₄Cl₂ at 25 °C. The curve shows the fit of the experimental data to a 1:1 binding profile.