
Jurgen Scheeder, 1 Johan F. J. Engbersen, 1 Alessandro Casmati, 2 Rocco Ungaro, 2 and David N. Reinholdt 2,6

Laboratory of Organic Chemistry, University of Twente, P.O. Box 217, 7500 AE, Enschede, The Netherlands, and Instituto di Chimica di Organica e Industriale, Università degli Studi, Viale delle Scienze, I-43100, Parma, Italy

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Two neutral receptors for halide anions and tricarboxylic anions have been synthesized on the basis of p-tert-butylcalix[6]arenes, symmetrically functionalized with three butyl(phenyl)urea groups at the 1,3,5-phenolic positions. The anion complexation has been studied by H NMR titration experiments, PTIR spectroscopy, and FAB mass spectrometry. The receptors bind halide and tricarboxylic anions exclusively through hydrogen bonding in a 1:1 fashion in DCM. For halide anions, a preference for bromide over chloride is observed, with a highest binding constant \( K_b \) of \( 1.4 \times 10^4 \) M\(^{-1} \) with receptor 4 containing the urea moieties. Thiourea receptor 5 most strongly binds 1,3,5-benzenetricarboxylic anions (\( K_b = 2.9 \times 10^4 \) M\(^{-1} \)) whereas 1,2,4- and 1,2,3-benzenetricarboxylic anions are complexed better by receptor 4 (\( K_b = 2.3 \times 10^4 \) and \( 4.7 \times 10^4 \) M\(^{-1} \), respectively). An explanation for the difference in the binding of halide and tricarboxylic anions by 4 and 5 is given. The mode of binding in the complex of 5 with 1,3,5-benzenetricarboxylic anion was elucidated by low-temperature NOEESY spectroscopy.

Introduction

In relation to our research on membrane transport 1 and sensors based on chemically modified field effect transistors (CHEMFETS), 3 we have developed various receptors for cations based on p-tert-butylcalix[4]arenes. One of the remaining challenges is the selective transport and detection of anions, but this requires selective anion receptors. The most straightforward method for the complexation of anions is by positively charged receptors which bind primarily via electrostatic interactions. A variety of polyaminium receptors 4 and guanidinium-based receptors 5 have been developed for the complexation of mono- and dicarboxylic anions 6,7,8 among others. The disadvantage of positively charged receptors is that the selectivity is generally modest due to the dominant nondirectional electrostatic interactions. This disadvantage can be overcome by the use of neutral anion receptors. Covalently incorporated Lewis acids like Si(IV), B(III), Al(III), Ge(IV), or Hg(II) in neutral ligands resulted in the complexation of anions via ion–dipole interactions. The disadvantage of these receptors is, however, the limited synthetic flexibility for varying or optimizing the selectivity of anion complexation. Recently, 6,10 we have shown that additional binding sites near a Lewis acid binding center, e.g., groups that provide hydrogen bond donors to the anionic guest, can increase the selectivity of anion complexation. Neutral uranylsalenes with additional hydrogen bond donating amide groups showed high selectivity in the complexation of HPO<sub>4</sub><sup>-</sup>. From the crystal structure of sulfamate 11 and phosphate 12 binding proteins, it is known that anions can be complexed with a high selectivity exclusively via formation of hydrogen bonds in a neutral binding site.

Calix[4]arenes have proven to be versatile molecular building blocks for the construction of selective receptors for cations 6,15 and neutral molecules. 14 We have reported the selective complexation of HSO<sub>4</sub><sup>-</sup> exclusively through hydrogen bonding by a neutral calix[4]arene with four

1 University of Twente.
2 Università degli Studi.
sulfonamide groups at the upper rim,\textsuperscript{16} and recently we have shown that the functionalization of the lower rim of calix[6]arenes with thiourea moieties facilitated the complexation of halide anions exclusively through hydrogen bonding.\textsuperscript{16,17} Hitherto, calix[6]arenes have received less attention as molecular building blocks, mainly because it is more difficult to control their conformation and the methods for the selective functionalization of the upper\textsuperscript{16} and lower rims\textsuperscript{16} are less well developed. Substitution of the phenolic positions with large alkyl or aryl groups is not sufficient to restrict the conformational motion in p-tert-butylicalix[6]arenes because we and others have recently shown that the tert-butylicalix[6]arene can rotate through the annulus.\textsuperscript{20,21} However, we have found that in 1,3,5-trimethoxy-2,4,6-trialkoxy-p-tert-butylicalix[6]arene the methoxy groups stabilize the cavity of the macrocycle via CH...Cl interactions.\textsuperscript{20} The 1,3,5-trimethoxy-2,4,6-tri(2-thiouracil)p-tert-butylicalix[6]arene adopts a flattened cone conformation with the three phenols in a syn,trans,trans position (u, u, u, o, o, o)\textsuperscript{22} and has C\textsubscript{3} symmetry. The remaining phenolic positions can be used to cap 1,3,5-trimethoxy-2,4,6-trihydroxy-p-tert-butylicalix[6]arene with a cyclohexylpentyl (CTVP) moiety, yielding a calix[6]arene derivative in a fixed C\textsubscript{3} symmetry.\textsuperscript{23,24}

Here, we report the synthesis and the binding properties of two p-tert-butylicalix[6]arene derivatives, 4 and 5, functionalized with three urea or thiourea moieties, respectively (Scheme 1). These molecules can function as neutral ligands for anions, and the anion recognition occurs exclusively through hydrogen bonding. These p-tert-butylicalix[6]arenes show selective binding of Br\textsuperscript{-} or Cl\textsuperscript{-} in chloroform solution and exhibit a high affinity for tricarboxylate anions. Several synthetic neutral receptors for mono- and dicarboxylate anions have been reported in which the binding site consists of a (thi)urea moiety.\textsuperscript{25-28} Wilcox et al.\textsuperscript{29} Hamilton et al.\textsuperscript{30} and Rebek et al.\textsuperscript{31} have used (thi)urea moieties to complex

\begin{enumerate}
\item[(18)] Muratomi, H.; Shinkai, S. J. \textit{Chem. Soc., Commun.} \textbf{1993}, \textit{1533}.
\item[(25)] de Mendoza, J.; Carramolino, M.; Cuevas, P.; Nieto, P. M.; Prados, P.; Reinholdt, D. N.; Verboom, W.; Ungaro, R.; Casnati, A. \textit{Synthesis} \textbf{1994}, \textit{43}.
\end{enumerate}
mono- and dicarboxylate anions in chloroform. Recently, Kelly and Kim\textsuperscript{26} reported the complexation of mono- and dicarboxylate anions and their isoterer by nonurea- and diurea-functionalized clfts.

**Results and Discussion**

Previously, we have shown that neutral receptors with hydrogen bond donors selectively bind anions (H\textsubscript{2}PO\textsubscript{4}\textsuperscript{-}, HSO\textsubscript{4}\textsuperscript{-},\textsuperscript{16} and halide anions\textsuperscript{16}) exclusively through hydrogen bonding. A strategy to organize hydrogen bond donating sites on calix[6]arene requires functionalization of 1,3,5-trimethoxy-2,4,6-trihydroxy-p-tert-butylcalix[6]-arene with three (thio)ureaalkyl groups. This will give a receptor with C\textsubscript{3} symmetry, and such a receptor would possibly complex, besides spherical anions, anions with C\textsubscript{3} symmetry.

The three phenolic oxygens of the starting compound, 1,3,5-trimethoxy-2,4,6-trihydroxy-p-tert-butylcalix[6]-arene (1),\textsuperscript{16,25} were alkylated using 6 equiv of NaN\textsubscript{3} and 4-bromobutyronitrile in DMP at 75 °C (Scheme 1).

The \textsuperscript{1}H NMR spectrum of the resulting product, 1,3,5-trimethoxy-2,4,6-tris(cyanopropoxy)-p-tert-butylcalix[6]arene (2), in CDCl\textsubscript{3} showed coalescence of the bridging methylene protons at room temperature and the corresponding \textsuperscript{13}C NMR spectrum showed a triplet at 30.3 ppm for the corresponding methylene carbon atoms. These results indicate that the compound is in a dynamic flattened cone conformation.\textsuperscript{20,21,22} Reduction of the cyanogroups using NaBH\textsubscript{4}/CoCl\textsubscript{2} in MeOH at room temperature\textsuperscript{23} yielded the 1,3,5-trimethoxy-2,4,6-tris(nitrobenzylxyloxy)-p-tert-butylcalix[6]arene (3), which is also in the flattened cone conformation at room temperature. Addition of 3.3 equiv of phenyl isothiocyanate to 3 in CHCl\textsubscript{3} at room temperature\textsuperscript{24} gave the corresponding phenylurea derivative 4 and phenylthiourea derivative 5 in 46% and 33% yield, respectively. These compounds are in the flattened cone conformation\textsuperscript{20,21} as could be concluded from the pair of doublets for the methylene protons in the \textsuperscript{1}H NMR spectrum at 4.43 and 3.80 ppm in 4 and at 4.46 and 3.34 ppm in 5, respectively, and the triplet at 29.8 ppm in 4 and 26.6 ppm in 5 for the corresponding methylene carbon atoms in the \textsuperscript{13}C NMR spectrum.\textsuperscript{22,25} The urea hydrogen of the phenylurea derivative 4 absorb at 7.79 ppm (NH\textsubscript{3}) and 5.70 ppm (NH\textsubscript{3}) and for the corresponding phenylthiourea hydrogens at 7.76 ppm (NH\textsubscript{3}) and 6.37 ppm (NH\textsubscript{3}). This difference in chemical shift indicates that the thiourea hydrogens are more acidic than the urea hydrogens, which is in accordance with the pK\textsubscript{a} values for thiourea and urea as reported in the literature\textsuperscript{26} (23.0 and 26.9, respectively).

As was established by Miodo,\textsuperscript{37} N,N'-disubstituted urea derivatives adopt the trans-trans geometry as drawn for 4 and 5 in Scheme 1. This geometry is also the only geometry observed in all crystal structures of N,N'-disubstituted urea derivatives reported in literature.\textsuperscript{8}

**Complexation of Br\textsuperscript{-} and Cl\textsuperscript{-} Anions.** Proper orientation of two or four (thio)urea moieties on a calix[4]arene platform enabled the complexation of spherical anions.\textsuperscript{16} Significant complexation of Cl\textsuperscript{-} and Br\textsuperscript{-} and weak complexation of I\textsuperscript{-}, CN\textsuperscript{-}, and SCN\textsuperscript{-} ions was observed. Therefore binding experiments with 4 and 5 were first carried out with Cl\textsuperscript{-} and Br\textsuperscript{-}. The negative FAB mass spectra of 1:1 mixtures of 4 or 5 with Bu\textsubscript{4}NCl or Bu\textsubscript{4}NBr in o-nitrophenyl octyl ether showed the anion complexes [4+Cl\textsuperscript{-}], [4+Br\textsuperscript{-}], [5+Cl\textsuperscript{-}], and [5+Br\textsuperscript{-}], besides the free ligands [4-H\textsuperscript{+}] and [5-H\textsuperscript{+}].

The \textsuperscript{1}H NMR spectra of 4 and 5 (CDCl\textsubscript{3}) show a downfield shift of the (thio)urea hydrogens upon the addition of Br\textsuperscript{-} and Cl\textsuperscript{-} (as their tetrabutylammonium salts), indicating the formation of hydrogen bonds to the halide guests. In addition, the ortho protons of the phenyl substituents at the (thio)urea groups show a downfield shift (0.07–0.09 ppm), whereas the meta and para protons shift upfield (meta 0.03–0.05 ppm; para 0.03 ppm). This effect may be attributed to a different electron density at the ortho and the meta and para positions of the aromatic ring due to the presence of the anionic guest.

In all cases \textsuperscript{1}H NMR titration experiments in CDCl\textsubscript{3} revealed a 1:1 stoichiometry of complexation as was proven by Job plot analysis (Figure 1).\textsuperscript{36–41} The association constants calculated from the changes in chemical shifts of the NH\textsubscript{3} hydrogens are summarized in Table 1.\textsuperscript{42}

**Figure 1.** Job plot of the titration of 5 mM Bu\textsubscript{4}NBr in CDCl\textsubscript{3} with 5 mM 4 in CDCl\textsubscript{3}.
Table 1. Association Constants ($K_a$, M$^{-1}$) and Free Energies of Association ($\Delta G^\circ$, kJ mol$^{-1}$) of Hosts 4 and 5 with Cl$^-$ and Br$^-$

<table>
<thead>
<tr>
<th>guest</th>
<th>$K_a$</th>
<th>$-\Delta G^\circ$</th>
<th>$K_a$</th>
<th>$-\Delta G^\circ$</th>
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<tr>
<td>Cl$^-$</td>
<td>480</td>
<td>15.1</td>
<td>28</td>
<td>7.9</td>
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<tr>
<td>Br$^-$</td>
<td>1450</td>
<td>17.8</td>
<td>390</td>
<td>14.3</td>
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</table>

* In CDCl$_3$, at 22 °C; concentration of host and guests are 5 mM. Guests are added as tetrabutylammonium salts.

Both Cl$^-$ and Br$^-$ are complexed more strongly by the urea host 4 than by the thiourea host 5, and both host compounds bind bromide in preference over chloride. Chloride induces a larger downfield shift of both (thio)urea hydrogens of 4 and 5 than bromide. For example, addition of 9 equiv of Bu$_4$NCl to 4 caused a downfield shift of 1.20 ppm for the NH$_3^+$ hydrogens, whereas addition of the same amount of Bu$_4$NBr gave a downfield shift of 0.75 ppm. With thioureas these values were 1.18 ppm for Bu$_4$NCl and 0.41 ppm for Bu$_4$NBr. The preference for Br$^-$ suggests that the cavity formed by the three (thio)urea moieties is more complementary to the size of the Br$^-$ anion than to that of Cl$^-$. Apparently, this better fit dominates the expected higher hydrogen bonding affinity of the hard Cl$^-$ anions for the hard (thio)urea hydrogens. This size selectivity is rather unexpected for this type of hosts, having rather flexible ligating sites, but it is a well-known phenomenon in anion complexation by positively charged receptors.

It was interesting to investigate whether these receptors would be selective for nitrate anions, having a 3-fold symmetry axis. The complexation of NO$_3^-$ by 4 and 5 was indeed observed in FAB mass spectrometry and $^1$H NMR. Unfortunately, quantitative determination of the association constants was not possible since the signals of the (thio)urea hydrogens became too broad upon the addition of nitrate and those of the phenyl substituent at the (thio)urea moiety coincide with the signals of the calix[6]arene aromatic rings.

Complexation of Tricarboxylate Anions. Complexation of carboxylate anions by (thio)urea receptors might benefit from favorable secondary electrostatic interactions between the partially positively charged (thio)urea hydrogens and the partially negatively charged oxygen atoms of the carboxylic acid group. Receptors 4 and 5 have three (thio)urea moieties arranged around a C$_3$ axis of symmetry. Benzenedicarboxylate anions with different symmetries, i.e. 1,3,5-benzenetricarboxylate 6 (trianion of trimesic acid), 1,2,4-benzenetricarboxylate 7 (trianion of trimellitic acid), and 1,2,3-benzenetricarboxylate 8 (trianion of hemimellitic acid) were studied (Chart 1).

For comparison, the monobasic anion benzoate 10, the dibasic anion isophthalate 11, and the nonplanar cis-1,3,5-cyclohexanetricarboxylate 9 were included.

Figure 2. Job plot of the titration of 5 mM (Bu$_4$N)$_2$6 in CDCl$_3$ with 5 mM 6 in CDCl$_3$.

Chart 1

1. 2. 3. 4. 5. 6. 7. 8. 9. 10. 11.

Table 2. Association Constants ($K_a$, M$^{-1}$) and Free Energies of Association ($\Delta G^\circ$, kJ mol$^{-1}$) of Hosts 4 and 5 with Guests 6–11

<table>
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<tr>
<th>guest</th>
<th>$K_a$</th>
<th>$-\Delta G^\circ$</th>
<th>$K_a$</th>
<th>$-\Delta G^\circ$</th>
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<td>6</td>
<td>57.000</td>
<td>27.9</td>
<td>290.000</td>
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<td>23.8</td>
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<td>17.8</td>
</tr>
<tr>
<td>11</td>
<td>69.000</td>
<td>27.3</td>
<td>6.400</td>
<td>21.5</td>
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* In CDCl$_3$, at 22 °C; concentration of host and guest are 5 mM. Guests are added as tetrabutylammonium salts.

The negative FAB mass spectra of 1:1 mixtures of 4 or 5 with (Bu$_4$N)$_3$-1,3,5-benzenetricarboxylate in o-nitrophenyl octyl ether showed the anion complexes [4+5$^-$] and [5+5$^-$/5$^-$] besides the free ligands [4-H$^+$] and [5-H$^+$]. $^1$H NMR titration experiments of 4 and 5 with the tetrabutylammonium salts of 6–11 in CDCl$_3$ revealed in all cases a 1:1 stoichiometry as was proven by Job plot analysis (Figure 2). The association constants are summarized in Table 2.

For the determination of the association constants the chemical shifts of the ortho protons of the phenyl sub-

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(45) The reduction of the 6–11 was followed over a range of 13–99% complex formed.
stituent at the (thi)urea groups were used. Also for these triamionic guests, the induced polarization in the phenyl ring decreases the electron density at the ortho positions in the phenyl ring (downfield shift) and increases the electron density at the meta and para positions (upfield shift). The signals for the NH\textsuperscript{a} and the NH\textsuperscript{b} hydrogens become broad upon the addition of carbonylate anions. A possible explanation of the broadening is a slow rotation of the guest in the complex around the C\textsubscript{3} axis.

The guest with C\textsubscript{3} symmetry, 1,3,5-benzenetricarbonyl-6, shows the strongest association with both 4 (K\textsubscript{d} = 8.7 \times 10\textsuperscript{5} M\textsuperscript{-1}) and 5 (K\textsubscript{d} = 2.9 \times 10\textsuperscript{6} M\textsuperscript{-1}). The 1,3,5-benzenetricarbonyl anion is rather planar\textsuperscript{26} with the carbonylate groups and the benzene ring in conjugation. The strongest complex is formed between the thiourea host 5, which is in accordance with the higher acidity of the thiourea. The tricarbonylate anion 6 is, due to its symmetrical and planar structure, the only guest species which can bind with all six hydrogen bond donating sites of the thiourea moieties of the host 5 (Chart 3, vide infra). Anions which do not have C\textsubscript{3} symmetry (7 and 8) bind to a lesser extent to both receptors. Also the monosubstituted carbonylates 10 and 11 show weaker complexation. The Job plot of the complexation of 10 by 4 and 5 is not symmetric, indicating that for this monobasic acid besides 1:1 association complexation with higher stoichiometries also occurs. The symmetrical cis-1,3,5-cyclohexanetricarbonyl 9 is complexed both by 4 and 5 in preference over the nonsymmetrical guests 7 and 8. This indicates that the complementarity of the C\textsubscript{3} symmetry of host and guest is important. The weaker binding between hosts 4 and 5 with the tricarbonylates 7 and 8 may be due to the nonplanarity of the carbonylate groups and the aromatic ring in 7 and 8.\textsuperscript{61}

All tricarbonylate anions 6–9 are complexed to a much greater degree than the halide anions because the halide shares only one unit of negative charge with three (thio)-urea moieties. In addition to the higher charge density in the tricarbonylate anions, electrostatic interactions between the carbonylate and the (thio)urea moieties contribute to the binding\textsuperscript{44} and the carbonylate anion group is structurally complementary with the (thio)urea moiety.

To investigate the difference in binding between urea host 4 and thiourea host 5 the model compounds 12 and \textsuperscript{40} The previous reported association constants for the complexation of carbonylate anions by neutral urea functionalized receptors are based on the change in chemical shift of the urea hydrogens.\textsuperscript{48–49}

\textsuperscript{47} The broadening is not caused by proton transfer of the (thio)urea moiety to the carbonylate groups since the pK\textsubscript{a} values of the tricarbonylic acids (pK\textsubscript{a}(4) = 11.9, pK\textsubscript{a}(5) = 11.0) are more than 10 decades lower than the pK\textsubscript{a} values of urea and thiourea (pK\textsubscript{a}(urea) = 26.9; pK\textsubscript{a}(thiourea) = 20.0).\textsuperscript{50}


\textsuperscript{49} This value is at the limit of the K\textsubscript{d} values that can be determined accurately by \textsuperscript{1}H NMR spectroscopy. Because a good fit for the regression procedure is obtained and the calculated value for the chemical shift at infinite excess of guest is within 0.06 ppm of the measured values for the chemical shift at large excess of guest present, the K\textsubscript{d} values calculated are accurate.

\textsuperscript{50} One of the carbonylic acid groups is rotated 27° out of the plane of the benzene ring; the other two are almost planar. Duchemp, D. J., Marsh, R. B. Acta Crystallogr. 1969, B25, 5.

\textsuperscript{51} (a) In 1,2,4-benzenetricarbonylic acid one of the carbonylic acid groups is rotated 96° out of the plane; the other two are rotated 6° and 9° out of the plane of the benzene ring. Takanaga, P.; Hirota, K.; Shimada, A. Bull. Chem. Soc. Jpn. 1978, 50, 2060. (b) In 1,2,3-benzenetricarbonylic acid one of the carbonylic acid groups is rotated 26.8° out of the plane; the other two are rotated 4.5° and 10.9° out of the plane. Takanaga, P.; Shimada, A. Ibid. 1988.


\textsuperscript{53} \textsuperscript{1}H NMR dilution experiments of 4 and 5 showed small downfield shifts of the (thio)urea hydrogens and no deuterium exchange could be obtained. The small downfield shifts may result from the fact that upon increasing the concentration of the host the intramolecular association decreases but the intramolecular association increases. This will result in a small overall effect on the chemical shifts of the (thio)urea hydrogens.


\textsuperscript{55} The non-hydrogen-bonded stretching frequency in N,N'-diaryleurea is found at ca. 3412 cm\textsuperscript{-1} in CHCl\textsubscript{3}.\textsuperscript{26} According to molecular models the NH–\textendash\textendash NH hydrogen bonding is possible as was also observed in the urea-derivatized calix[4]arenes.\textsuperscript{16}
the hydrogen-bonded NH stretching. \(N,N'\)-Diaryl- and \(N,N'\)-diarylihydroxamic compounds can exist as a mixture of trans-trans, cis-trans, and cis-cis geometries in CHCl\(_3\) solution.\(^{66}\) Thiourea host 5 shows sharp bands at 3410 and 3394 cm\(^{-1}\). In principle, these bands could result from the presence of trans-trans, cis-cis, and trans-cis geometries. However, for anion binding the trans-trans geometry is desired. Upon the addition of anions these two bands are retained, indicating that the same geometry, the trans-trans geometry, is present in the free ligand 5 and the anion complexes of 5. Consequently, these bands are attributed to non-hydrogen-bonded NH stretching and to weak NH--\(\cdot\)\(\cdot\)\(\cdot\) NH hydrogen bonding, respectively. The weak, broad band at 3309 cm\(^{-1}\) originates from hydrogen-bonded NH stretching in the free ligand 5. The difference in the hydrogen-bonded stretching frequencies of 4 and 5 is 38 cm\(^{-1}\), resulting from the higher acidity of the thiourea hydrogens.

Allerhand and Schleyer\(^{57}\) showed that the role of halide anions as hydrogen bond acceptors can be studied by FTIR spectroscopy. To study the effect of anion complexation, the infrared spectra of the 1:1 mixture of host 4 and 5 with Bu\(_4\)NCl, Bu\(_4\)NBr, and the tetraethylammonium salts of carboxylates 6–11 in CDCl\(_3\) were investigated (Table 3).

Upon addition of 1 equiv of Cl\(^{-}\) or Br\(^{-}\) to 4, the bands of the free ligand disappear and two new absorption bands appear, a sharp band at 3393 cm\(^{-1}\), attributed to weak NH--\(\cdot\)\(\cdot\)\(\cdot\) NH hydrogen bonding, and a more intense, broad band at 3336 cm\(^{-1}\), attributed to hydrogen bonding to the halide anion. Addition of 1 equiv of Cl\(^{-}\) or Br\(^{-}\) to 5 results in a decrease of the bands at 3410 and 3394 cm\(^{-1}\) and complete disappearance of the band at 3309 cm\(^{-1}\). A new, broad band at 3275 cm\(^{-1}\) appears, indicating hydrogen bonding to the anion. However, unlike the halide complex of 4, in the halide complex of 5 the absorption due to the non-hydrogen-bonded NH and the NH--\(\cdot\)\(\cdot\)\(\cdot\) NH hydrogen bonding are still present. Addition of 1 equiv of carboxylate anions 6–11 to 4 results in the disappearance of the band at 3403 cm\(^{-1}\) and the appearance of two sharp bands at 3420 and 3391 cm\(^{-1}\), attributed to a non-hydrogen-bonded NH stretch and NH--\(\cdot\)\(\cdot\)\(\cdot\) NH hydrogen bonding, respectively, and a broad band at around 3310 cm\(^{-1}\), attributed to hydrogen bonding to the anionic guests. In case of 5, addition of carboxylate anions results in a decrease of the intensity of the bands at 3420 and 3392 cm\(^{-1}\) and the appearance of a broad band at 3275 cm\(^{-1}\) due to hydrogen bonding to the guests. The intensity of this band is higher than in the presence of halide anions, indicating stronger hydrogen bonding to the carboxylate anions.

**Structure of the Complex of Thiourea Host 5 with 1,3,5-Benzentricarboxylate 6 in Solution.** To obtain the highest resonance stabilization in the complex of host 5 and guest 6, the carboxylate groups are probably in the plane of the aromatic ring. This implies that the carboxylate groups in the complex are directed perpendicular to the plane through the thiourea moieties. In this case two different arrangements of hydrogen bond formations are possible. The first possibility is that the two oxygen atoms of a carboxylate group are facing toward the NH donor sites of a thiourea moiety in a perpendicular orientation, forming three centered hydrogen bonds by each donor and acceptor site (Chart 3). The second possibility is that the thiourea groups lie around the 1,3,5-benzentricarboxylate anion and in plane with benzene ring. However, NOESY spectroscopy in CDCl\(_3\) at \(-50^\circ\)C showed clear NOE contacts between the aromatic protons of carboxylate 6 and the ortho protons of the phenyl substituent and the CH\(_2\)NH\(^{+}\) protons of the spacer of host 5. This indicates that the guest is in between the phenyl substituent at the thiourea moieties and the spacer. In the complex the anion is bound via 12 three-centered hydrogen bonds (Chart 3). Three centered hydrogen bonds are preferred when there are relatively few hydrogen bond donors.\(^{56}\)

**Conclusions**

The p-tert-butylicalix[6]arenes derivatized with three \(N'\)-phenyl-N-butylurea or \(N'\)-phenyl-N-butyliothiourea groups at the 2,4,6-phenolic positions, 4 and 5, represent a new class of neutral receptors for halide and tricarboxylate anions in which the binding occurs exclusively through hydrogen bonding. The stoichiometry of the complex formation is 1:1, and the selectivity for halide anions is Br\(^{-}\) > Cl\(^{-}\). The 3-fold axis of symmetry of the binding sites in the hosts leads to a preference for complexation of the symmetrical 1,3,5-benzentricarboxylate anion 6.

**Experimental Section\(^{59}\)**

p-tert-Butylicalix[6]arene\(^{59}\) and 1,3,5-trimethoxy-2,4,6-tri-hydroxy-p-tert-butylicalix[6]arene\(^{39}\) (1) have been prepared according to literature procedures. FTIR spectra were recorded in 10 mM CDCl\(_3\) solutions on a BIORAD FTIR spectrometer. FAB mass spectra were obtained with a Finnigan MAT90 mass spectrometer equipped with a PDP 11/73 data system using m-nitrobenzyl alcohol (NBA) as a matrix. The measurements were carried out using an Ion Tech atom gun unit, operating at 8 kV and 1 mA. The spectra and

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\(^{59}\) For general experimental procedures and procedures concerning the \(^1\)H NMR titration experiments see ref 16.

intensity lists (averaged from three scans) were obtained in the negative and positive mode. For the measurements, 1 mg of sample was dissolved in 2 μL of NBOA on the vacuum chamber target. The ions, produced by bombardment with a beam of xenon gas, were accelerated with a voltage of 5 kV. NOESY spectra were recorded on a Varian 400 MHz spectrometer at -50 °C in CDCl3.

5.11,17,23,29,35-Hexa-p-tart-buty1-37,39,41-tris[(cyanopropoxy)oxyl]38,40,42-trimethoxyalicyl][arene (3). NaH (0.36 g, 9.0 mmol) and calix[6]arene (1.14 g, 1.13 mmol) in DMF (55 mL) were stirred for 1 h at room temperature. 4-Butyrotritile (0.68 mL, 7.75 mmol) was added, and the mixture was stirred at 75 °C during 3.5 h. DMF was evaporated, and the residue was taken up in CH2Cl2 (100 mL), washed with 1 N HCl (50 mL, 2x), saturated NH4Cl (50 mL, 3x), and brine (50 mL), and dried with MgSO4. Filtration followed by evaporation of the solvent gave the crude product, which was triturated with MeOH to yield 82%; mp 235–236 °C. IR (KBr): 3246 cm-1 (CN). 1H NMR: δ 7.11 and 6.29 (6H, Hi), 3.90 (6H, Hi), 3.74 (6H, Hi), 2.89 (8H, H2), 2.53 (6H, H2), 2.14 (6H, H2), 1.15 (6H, H2), and 0.98 (6H, 27 H). 13C NMR: δ 154.0 (a), 151.7 (a), 150.7 (a), 145.5 (a), 139.5 (d), 133.3 (d), 127.0 (a), 122.0 (a), 118.7 (CN), 70.1 (2), 60.2 (q), 54.2 (a), 34.1 (a), 31.5 (q), 20.4 (q), 19.8 (q), 14.5 (q), FAB mass spectrum, m/z 1216.8 (M+), calc. 1216.8.

Commercially obtained CaSO4 was used. CaCl2 (30 g, 0.34 mol) was added to the mixture. CaCO3 (20 g, 0.33 mol) was added, and the mixture was stirred for 1 h at room temperature. The mixture was filtered, and the filtrate was evaporated. The residue was taken up in CH2Cl2 (100 mL), and the organic layer was washed with H2O (50 mL) and brine (50 mL) and dried with Na2SO4. Evaporation of the solvent yielded a slightly colored foam that was used immediately for further reactions. Yield 96%; mp 220–221 °C. IR (KBr): 3084 (ν(C=O)), 1655 (C=O), 1561 (C=O), 1434 (C=O), 1309 (C=O), 1210 (C=O), 1099 (C=O), 835 (C=O), 760 (C=O), 692 (C=O).

Preparation of the Tributylammonium Salts of Carbonylic Acids 6–11. A mixture of the carboxylic acid (6 mmol) in 1 M Bu4NOH solution in MeOH (15, 10, or 5 mL) was stirred for 1 h at room temperature. The solvent was evaporated, and the product was dried at high vacuum over P2O5.

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