ANION RECEPTORS

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Abstract – The review outlines the recent achievements in the field of anion coordination chemistry, and is focusing on the function-oriented design of anion-binding “host” ligands. Comparative analysis of receptor abilities for various classes of organic compounds towards anions is presented.

Introduction

1. Molecular recognition of spherical anions
   1.1. Complexes with the fluoride anion
   1.2. Binding of chloride and bromide anions
   1.3. Iodide recognition
2. Coordination chemistry of nonspherical anions
   2.1. Binding of linear anions (CN−, N3−)
   2.2. Complexation with planar anion species (RCOO−, NO3−)
   2.3. Sensors for tetrahedral anions (H2PO4−, HSO4−, Cr2O72−, ReO4−, TcO4−)

Conclusion

INTRODUCTION

In spite of the fact that anions play an important role in chemistry1 and biology,2 the coordination chemistry of anions has not received much attention in comparison with the design of “host” ligands for cations and neutral species,3 although a number of publications dealing with anion ligands increased considerably during the last decade.4-7 This field is of special interest because of a plausible use of anion

This paper is dedicated to the memory of the Emeritus Professor Kenji Koga of Tokyo University.
receptors in biology, medicine and catalysis. The previously published reviews concerned the ability of organic receptors towards a wide range of anions. The aim of this review is to focus on the function-oriented design of anion-binding “host” ligands and to show which functional groups must be present in molecules in order to obtain compounds which are specific for coordination with this or that particular group of anions.

Anions are known to feature a relatively large size. Therefore, they require receptors of considerably bigger size than ligands for cations. Moreover, anions may exists in a range of geometrical shapes, e.g. spherical (halides), linear (SCN⁻, N₃⁻), planar (COO⁻, NO₃⁻), tetrahedral (H₂PO₄⁻, HSO₄⁻, Cr₂O₇²⁻). Both neutral and positively charged “host” ligands can be used for anion binding. Binding sites, which are able to form N⁺-H···X⁻ hydrogen bonds appear to be the most important and regular fragments which are used to design anion receptors. Therefore, it is not surprising at all that there are a variety of compounds capable of anion recognition, such as amides, ureas, perfluorinated compounds, cryptands and complexes with metals.

1. MOLECULAR RECOGNITION OF SPHERICAL ANIONS

Stability of complexes, as well as selectivity of ligands towards anions depend on both electrostatic and structural factors. Only those compounds, molecular cavities of which do correspond to ionic radius of anions, and are structurally able to form hydrogen bonds with spherical anions seem to be appropriate ligands.

The most striking example is the rhenium complex of polypyridyl-containing ligand (1) exhibiting a high affinity to halides (K (F⁻) = 3.82 · 10⁵ M⁻¹, K (Cl⁻) = 4 · 10⁴ M⁻¹, K (Br⁻) = 4 · 10⁴ M⁻¹, K (I⁻) = 1.49 · 10⁵ M⁻¹).\(^{11}\)

![Diagram of Compound (1)](image)

Compound (1) shows a strong binding affinity towards halides since several factors contribute to the complex formation: electrostatic force, hydrogen bonding and steric effects.
1.1. COMPLEXES WITH THE FLUORIDE ANION

High affinity of a boron atom to the fluoride anion suggests using of boron compounds as sensors. Indeed, triarylamines bearing one, two or three boronic ester groups were designed as the fluoride receptors. Compound (2) seems to be a very promising one because of high binding constant ($K = 10^7 \text{ M}^{-1}$) and excellent selectivity towards $F^-$. The same type of interaction takes place when the fluoride anion interacts with the receptor (3). In this case simultaneous coordination of the potassium cation with oxygen atoms of the crown ether facilitates binding of the fluoride anion with boron atom. It is interesting to note that attempts to use 3 as a ditopic receptor for KCl and KBr have failed, while the potassium cation does give a strong complex.

Imidazolidinium based receptor (4) exhibits an unique affinity and high selectivity towards the fluoride anion due to steric requirements and cooperative intramolecular binding ($K = 10^{13} \text{ M}^{-1}$).

Calix[4]pyrrole (5) belongs to another group of the fluoride receptors. It has been shown that interaction of calix[4]pyrrole with the fluoride anion is accompanied by the formation of four NH · · · F$^-$ hydrogen bonds and conformerization of the molecule from 1,3-alternate into the cone conformer.

High selectivity towards the fluoride anion ($K = 10^5 \text{ M}^{-1}$) relative to other halides ($K = 10^{-10^2} \text{ M}^{-1}$) makes calix[4]pyrrole to be rather selective F$^-$ binding agents. Also, it should be noted that while increasing a molecular cavity size, the order of selectivity is changed as follows: $F^- < Cl^- < Br^- < I^-$. 
It has been found that porphyrins and their metallated forms can be used for fluoride binding, and the mechanism of complex formation depends on porphyrin structure. Thus, porphyrin 6 coordinates with F\(^{-}\) by means of hydrogen bond formation \((K = 2.5 \cdot 10^5 - 2.6 \cdot 10^4 \text{ M}^{-1})\), while the complex 7 binds the fluoride anion through donor-acceptor mechanism \((K = 7.7 \cdot 10^2)\).\(^{20,21}\)

The strapped calix[4]pyrrole-metalloporphyrin conjugate (8), in which the calixpyrrole fragment is in the 1,3-alternate conformation exhibits a strong binding with the fluoride anion in organic solvents in the presence of Cl\(^{-}\), Br\(^{-}\) and I\(^{-}\).\(^{22}\)

Amides, ureas, thioureas and their cyclic derivatives (9 a-d) are appropriate ligands for selective complex formation with the fluoride anion due to strong hydrogen bonds (Table 1).
Table 1. Fluoride anion binding constants for receptors (9 a-d)

<table>
<thead>
<tr>
<th>No</th>
<th>Structure</th>
<th>$K$ (M$^{-1}$)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>9a</td>
<td><img src="image" alt="Structure" /></td>
<td>$10^4 \ (X = S) \div 8 \cdot 10^2 \ (X = O)$</td>
<td>[23]</td>
</tr>
<tr>
<td>9b</td>
<td><img src="image" alt="Structure" /></td>
<td>$2.5 \cdot 10^4 \ (R = CF_3)$&lt;br&gt;$6 \cdot 10^3 \ (R = H)$</td>
<td>[24]</td>
</tr>
<tr>
<td>9c</td>
<td><img src="image" alt="Structure" /></td>
<td>$2.5 \cdot 10^3$</td>
<td>[25, 26]</td>
</tr>
<tr>
<td>9d</td>
<td><img src="image" alt="Structure" /></td>
<td>$2 \cdot 10^1 \div 2.3 \cdot 10^2$</td>
<td>[27,28]</td>
</tr>
</tbody>
</table>

1.2. BINDING OF CHLORIDE AND BROMIDE ANIONS
Design of receptors for chlorides and bromides is based on the following requirements: *i*) molecular cavity of a “host” ligand has to be comparable with ionic radius of halide; *ii*) a possibility to form strong hydrogen bonds. Similarities in shape, ionic radius \( r(\text{Cl}^-) = 0.181; r(\text{Br}^-) = 0.196 \) and free energy values for chloride and bromide anions makes selective separation of these anions to be hardly possible. However, some amide-substituted ferrocenyl compounds are suitable for selective recognition of the chloride anion. It is suggested that the complex with both anion and solvent is formed, since solvent polarity affects binding constants greatly (Table 2).

**Table 2.** \( \text{Cl}^- \) anion binding constants, determined by \(^1\text{H} \) NMR spectra

<table>
<thead>
<tr>
<th>Receptor</th>
<th>CD(_2\text{Cl}_2)</th>
<th>(CD(_3\text{CO}_2)O)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Receptor" /></td>
<td>40</td>
<td>5.2 ( \times ) 10(^3)</td>
<td>[28]</td>
</tr>
<tr>
<td><img src="image2" alt="Receptor" /></td>
<td>1.75 ( \times ) 10(^2)</td>
<td>4 ( \times ) 10(^3)</td>
<td>[28]</td>
</tr>
</tbody>
</table>

Macrocycles containing amide and pyrrole moieties are also well known as receptors for \( \text{Cl}^- \). \(^{29,30}\)

The steroid-like ligand (10) was found to coordinate with the chloride anion more effectively than binding of \( \text{Br}^- \) \( (K = 10^6 \) and \( K=9.2 \times 10^4 \) respectively, in CDCl\(_3\)).\(^{31,32}\)
Also, calixarenes are of interest as chloride and bromide receptors. Modification at the upper ring of calixarenes with functional groups which are able to form strong hydrogen provides new possibilities for molecular design of anion receptors.

Sulfonamide calix[4]arenes (11) and (12) have been shown to form quite stable complexes with Cl⁻ ($K = 3.6 \cdot 10^2 \text{ M}^{-1}$), and incorporation of triazole or alkylamide fragments with additional binding centers proved to result in increase of not only molecular cavity size, but also binding constants ($K = 0.9 \cdot 10^3 \div 1.25 \cdot 10^3 \text{ M}^{-1}$).33, 34

A selective receptor for the bromide anion is exemplified by calixarene with a fluorine-containing substituent at the upper rim.35

Incorporation of urea and thiourea fragments into calixarenes is a common approach to build halide-binding ligands. However, without a permanent cavity these compounds are not selective towards anions of the same group of symmetry. Indeed, ureidocalixarenes have a high receptor ability, but a low selectivity towards chloride and bromide anions (Table 3).

**Table 3. Binding constants for some ureidocalixarenes**

<table>
<thead>
<tr>
<th>Calixarene</th>
<th>$K (\text{M}^{-1})$</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\text{Cl}^-$</td>
<td>$\text{Br}^-$</td>
</tr>
<tr>
<td></td>
<td>$7.1 \cdot 10^3$</td>
<td>$2.6 \cdot 10^3$</td>
</tr>
<tr>
<td>Calixarene</td>
<td>$K$ (M$^{-1}$)</td>
<td>Ref.</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------</td>
<td>------</td>
</tr>
<tr>
<td><img src="image1.png" alt="Calixarene 1" /></td>
<td>$4.7 \cdot 10^3$</td>
<td>$1.5 \cdot 10^3$</td>
</tr>
<tr>
<td><img src="image2.png" alt="Calixarene 2" /></td>
<td>$4.6 \cdot 10^3$</td>
<td>$1.4 \cdot 10^3$</td>
</tr>
<tr>
<td><img src="image3.png" alt="Calixarene 3" /></td>
<td>$2.5 \cdot 10^3$</td>
<td>$1.6 \cdot 10^3$</td>
</tr>
<tr>
<td><img src="image4.png" alt="Calixarene 4" /></td>
<td>$8.3 \cdot 10^2$</td>
<td>$2.8 \cdot 10^2$</td>
</tr>
<tr>
<td><img src="image5.png" alt="Calixarene 5" /></td>
<td>160</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>
1.4. IODIDE RECOGNITION

A low electronegative character of an iodine atom and a large ionic radius \( r = 0.220 \) are probably the main reasons that only a few highly selective receptors for the iodide anion have been designed. Thus, calix[5]pyrroles seem to be good ligands for selective binding of \( I^- \) \((K = 2.5 \times 10^4 \text{ M}^{-1})\). Also \( 13 \) proved to be an appropriate compound for iodide recognition \((K = 6.5 \times 10^3 \text{ M}^{-1})\).\(^4\)

2. COORDINATION CHEMISTRY OF NONSPHERICAL ANION

2.1. BINDING OF LINEAR ANIONS (\( \text{CN}^-, \text{N}_3^- \))

Complementarity of linear anions and energy binding depend on some intrinsic properties of anions, and the arrangement of binding sites in the “host” molecules. For instance, criptate (14) is not preorganised host, however it undergoes a conformational rearrangement on azide anion binding from \( \text{out, out} \) geometry into the \( \text{in, in} \) conformer. It binds anionic guest species via two pyramidal beams with \( {}^+\text{NH} \cdots \text{N}^- \) hydrogen bonds.\(^4\)
There are a few complexes with the cyanide anion in the series of both open-chain and cyclic systems bearing the 2,6-pyridyldicarbonyl fragment (Table 4).

**Table 4.** CN⁻ - Binding constants

<table>
<thead>
<tr>
<th>Structure</th>
<th>( K ) (M⁻¹)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.8 ( \times ) 10⁵</td>
<td>[11]</td>
</tr>
<tr>
<td></td>
<td>1.2 ( \times ) 10⁴</td>
<td>[43]</td>
</tr>
<tr>
<td></td>
<td>1.15 ( \times ) 10²</td>
<td>[44]</td>
</tr>
</tbody>
</table>

**2.2. COMPLEXATION WITH PLANAR ANION SPECIES (RCOO⁻, NO₃⁻ )**

From 70 to 75 % of enzyme substrates and cofactors are anions, very often they are presented by phosphates. Sulfates, carboxylates and nitrates are also wide-spreaded anions in biological systems. Design of receptors for such anions is of great importance.

Carboxylates can be binded with both polyammonium open-chain compounds and their macrocyclic analogues having various dimentions of complexation cavity. Selectivity of ligands and stability of their complexes depend on the structure and charge of both host and guest molecules (Table 5).

**Table 5.** Acetate binding constants for polyammonium receptors

<table>
<thead>
<tr>
<th>Receptor</th>
<th>MeCOO⁻</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>( X = S ) (a), ( O ) (b)</td>
<td>a) 1.4 ( \times ) 10⁴; b) 2.6 ( \times ) 10³</td>
<td>[23]</td>
</tr>
<tr>
<td></td>
<td>3.8 ( \times ) 10⁴</td>
<td>[43]</td>
</tr>
</tbody>
</table>
The guanidinium ion is undoubtedly a very popular motif in the design of anion hosts, because of its regular occurrence as a part of argenine in naturally occurring complexes. Receptors of this type are able to form two chelate bonds with the carboxylate anion. For instance, chiral guanidinium-type receptor (15) is able to recognize carboxylates and nucleotides due to multiple hydrogen bond interactions.\textsuperscript{45}

\begin{center}
\includegraphics[width=0.8\textwidth]{guanidinium.png}
\end{center}

A structural similarity between urea and guanidine suggests that ureido substituted compounds can also exhibit a high receptor ability towards carboxylates. Indeed, incorporation of urea or thiourea fragments into the structure of “host” ligands proved to change their physico-chemical properties, thus making these compounds to be appropriate agents for selective extraction of anions (Table 6).

Table 6. Acetate binding constants for ureido derivatives

<table>
<thead>
<tr>
<th>Receptor</th>
<th>AcO\textsuperscript{-}</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.2 \times 10\textsuperscript{3} M\textsuperscript{-1}</td>
<td>[48]</td>
</tr>
<tr>
<td></td>
<td>a) 7.9 \times 10\textsuperscript{2} M\textsuperscript{-1}</td>
<td>[23]</td>
</tr>
<tr>
<td></td>
<td>b) 1 \times 10\textsuperscript{4} M\textsuperscript{-1}</td>
<td>[49]</td>
</tr>
<tr>
<td></td>
<td>2.2 \times 10\textsuperscript{3} M\textsuperscript{-1}</td>
<td></td>
</tr>
</tbody>
</table>

Calix[4]arene bearing thiourea fragments was reported to bind the acetate anion preferentially to diphenylposphate, thus forming the corresponding complex with \( K = 1,1 \times 10\textsuperscript{3} \text{ M}^{-1} \).\textsuperscript{50}

Another example is the structure of calixarenes substituted with amidoferrocenyl units (16). These compounds are able to act as electrochemical sensors for carboxylate anions (Table 7).\textsuperscript{51} Planar
arrangement of substituents in 16 allows one to use it for selective binding of carboxylates in the presence of \( \text{H}_2\text{PO}_4^- \) and \( \text{Cl}^- \) anions.

**Table 7.** Binding constants for receptors (16)

<table>
<thead>
<tr>
<th>R</th>
<th>PhCOO(^-)</th>
<th>CH(_3)COO(^-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH(_3)</td>
<td>(5.4 \cdot 10^2 \text{ M}^{-1})</td>
<td>(8.26 \cdot 10^2 \text{ M}^{-1})</td>
</tr>
<tr>
<td>CH(_2)COOC(_2)H(_5)</td>
<td>(10^3 \text{ M}^{-1})</td>
<td>(1.2 \cdot 10^3 \text{ M}^{-1})</td>
</tr>
</tbody>
</table>

The reaction of tetra-\(p\)-formyltetra-\(O\)-propylcalix[4]arene with phenanthrenequinone in the presence of \(\text{NH}_4\text{OAc}\) has afforded a new type of calixarenes having an enlarged aromatic cavity stabilized by hydrogen-bonded bridges.\(^52\)

Porphyrins and relative compounds demonstrate their ability to coordinate with carboxylates both in solution and solid state (Table 8).\(^53\)

**Table 8.** Binding constants for porphyrin-containing receptors (17) and (18).

<table>
<thead>
<tr>
<th></th>
<th>CH(_3)COO(^-)</th>
<th>(3.3 \cdot 10^3)</th>
<th>(3 \cdot 10^5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref.</td>
<td>[21]</td>
<td>[20]</td>
<td></td>
</tr>
</tbody>
</table>

A few examples deal with the nitrate anion involved in the complex formation. The data available show that amide-containing receptors are often used for binding this group of anions (Table 9).
Table 9. Acetate binding constants

<table>
<thead>
<tr>
<th>Receptor</th>
<th>$K$ (M$^{-1}$)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Receptor 1" /></td>
<td>$6.3 \cdot 10^2$</td>
<td>[11]</td>
</tr>
<tr>
<td><img src="image2" alt="Receptor 2" /></td>
<td>$5.6 \cdot 10^2$</td>
<td>[54]</td>
</tr>
<tr>
<td><img src="image3" alt="Receptor 3" /></td>
<td>$5 \cdot 10^2$</td>
<td>[34]</td>
</tr>
<tr>
<td><img src="image4" alt="Receptor 4" /></td>
<td>$3 \cdot 10^2$</td>
<td>[44]</td>
</tr>
</tbody>
</table>
2.3. SENSORS FOR TETRAHEDRAL ANIONS (H$_2$PO$_4^-$, HSO$_4^-$, CR$_2$O$_7^{2-}$)

Phosphates as well as carboxylates are coordinated with polyammonium ligands regardless of their molecular cavity size (Table 10).

**Table 10.** Dihydrophosphate binding constants

<table>
<thead>
<tr>
<th>Receptor</th>
<th>H$_2$PO$_4^-$</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Receptor" /></td>
<td>a) $6.1 \cdot 10^3$ b) $1.4 \cdot 10^4$</td>
<td>[56]</td>
</tr>
<tr>
<td><img src="image2" alt="Receptor" /></td>
<td>$2 \cdot 10^3$</td>
<td>[29]</td>
</tr>
<tr>
<td><img src="image3" alt="Receptor" /></td>
<td>$3.4 \cdot 10^3$</td>
<td>[43]</td>
</tr>
</tbody>
</table>
Ureido substituted compounds are also suitable ligands for complexes with phosphate anions which are stabilized by NH⋯O⁻ hydrogen bond formation. (Table 11).

**Table 11.** Dihydrophosphate binding constants for (thio)ureido-containing ligands

<table>
<thead>
<tr>
<th>Receptor</th>
<th>$\text{H}_2\text{PO}_4^-$</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="structure1" /></td>
<td>a) $4 \cdot 10^3$ b) $1.7 \cdot 10^3$</td>
<td>[23]</td>
</tr>
<tr>
<td><img src="image2" alt="structure2" /></td>
<td>$1.5 \cdot 10^4$</td>
<td>[57]</td>
</tr>
<tr>
<td><img src="image3" alt="structure3" /></td>
<td>$1.95 \cdot 10^5$</td>
<td>[47]</td>
</tr>
<tr>
<td><img src="image4" alt="structure4" /></td>
<td>a) $7.9 \cdot 10^2$ b) $5 \cdot 10^3$</td>
<td>[23]</td>
</tr>
</tbody>
</table>
Porphyrine free bases (17) and (18), not metallated derivatives, are able to bind with the dihydrophosphate anion, again the crucial role belongs to NH · · · O− hydrogen bond formation. (Table 12).

According to the 1H NMR spectral data calix[4]pyrrole (5) interacts with H2PO4− to form 1:1 (ligand : anion) complex in acetonitrile and N,N-dimethylformamide through hydrogen bond formation.58

Table 12. Binding constants for porphyrin receptors (17) and (18)

<table>
<thead>
<tr>
<th>Receptor</th>
<th>H2PO4−</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 · 107</td>
<td>[23]</td>
</tr>
<tr>
<td></td>
<td>1.2 · 104</td>
<td>[49]</td>
</tr>
</tbody>
</table>

There are some examples of highly selective receptors for HSO4− anion. Again, the data available indicate that complex formation is rather sensitive to structural and charge characteristics of both host and guest molecules. For example, protonation of compound (19) results in the formation of diammonium salt (20) with much lower receptor ability relative to that one of the neutral species.59
Sulfonamoylcalix[4]arene (21) exhibits a selectivity for $\text{HSO}_4^-$ of about 100 over $\text{Cl}^-$ and $\text{NO}_3^-$.  

A few works deal with the formation of complexes with the bichromate anion. It has been established that sulfonamide-substituted calixarene coordinates with the bichromate anion through four hydrogen bonds.  

A few papers describe extraction of pertechnetate and perrhenate anions, which are of great interest for nuclear waste reprocessing. Calixarenes in both cone and 1,3-alternate conformation can be successfully used for that. Thus, it has been shown that calix[4]arene bis(crown-6) (22) in the 1,3-alternate conformation can extract pertechnetate anion from acidic or basic aqueous solution into an organic phase. Tetrasubstituted calix[4]arenes (22), containing carbonyl and ester groups and existing in a cone conformation proved to be selective and efficient extracting agents for Tc(VII) recognition. Calixarene (23) also exhibits a highly selective extraction of $\text{ReO}_4^-$ in the presence of a large amount of other anions. A vast majority of anions, such as $\text{Cl}^-$, $\text{Br}^-$, $\text{Ac}^-$, $\text{H}_2\text{PO}_4^-$ can be tolerated in the ratio 1 : 500, while $\text{NO}_3^-$ - in the ratio 1 : 400.
A new tripodal tris(amido benzo-15-crown-5) ligand binds perrhenate anions \((K = 8.4 \cdot 10^2 \text{ M}^{-1})\) cooperatively with the crown ether complexed with sodium cations.\(^{65}\)

**CONCLUSION**

Recognition of anionic guest species by synthetic ligands is a rapidly growing area of research. Indeed, many derivatives representing various classes of ligands capable of anion binding have been developed during the last decade. The data available in the literature show that amide-anion hydrogen bond interaction plays an important role in anion recognition in naturally occurring proteins and other biological systems. Also technical applications of the coordination chemistry of anions seem to be very promising.

**REFERENCES**


