Silver(I) Induced Conformational Change in a Molecular Clip.

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Abstract. Molecular clips with naphthalene walls change conformation upon binding of silver ions.

One of the interesting recent developments in molecular recognition is the construction of host molecules that change conformation upon binding of a guest molecule. Recent examples include the bis-crown ethers of Rebek\(^1\), the clamshell cyclodextrins of Breslow\(^2\), and the substituted calixarenes of Shinkai\(^3\). In previous papers we reported on molecular clips derived from diphenylglycoluril which contain large aromatic walls (see 1)\(^4\). Molecules 1 can adopt three conformations (ss, sa and aa, see Figure 1) which interconvert slowly on the NMR timescale. The aa conformer is capable of binding aromatic guests such as 1,3-dinitrobenzene and 1,4-dicyanobenzene by an induced-fit mechanism. In this communication we present evidence that silver ions are bound in 1 by a similar mechanism.

Clip molecule 1a was synthesised from diphenylglycoluril as described previously\(^4\). Compound 1b was prepared in the same way starting from dimethylglycoluril (overall yield 13%)\(^5\).

The NCH\(_2\) signals (H\(_{\text{in}}\) and H\(_{\text{out}}\), see 1) in the \(^1\)H-NMR spectra of the clips can be used to determine the relative amount of each conformer that is present in solution. Upon addition of the sparingly soluble salt
Figure 1 Binding of Ag+ by the aa and the ss conformers of clip 1a.

AgClO₄ to a solution of 1a in CDCl₃ an increase of the NMR signals of the aa conformer was observed. Subsequent titrations of this host with various silver salts in CD₃OD/CDCl₃ (1:9, v/v, to increase the solubility of the salts) revealed that not only the relative amount of aa conformer increased, but also that of the ss, suggesting that the latter is capable of binding a silver ion stronger than the sa conformer (see Figure 1). The results of different titration experiments are presented in Table 1. As can be seen, the values of Kaa and Kss strongly depend on the type of silver salt. A similar observation was made by Crookes et al in their studies on the complexation of different silver salts to ethylene. They explained the observed anion dependences by competition reactions between the anion and the ethylene for the Ag⁺-cation. Similar effects may also be operative in our system. The strength of the association constant for the silver-clip complex is correlated to the Ag⁺ anion interaction.

Table 1 Relative association constants (M⁻¹) for the complexation of silver salts in the aa and ss conformers of 1a (estimated error 15%).

<table>
<thead>
<tr>
<th>Silver salt</th>
<th>Kaa</th>
<th>Kss</th>
<th>Silver salt</th>
<th>Kaa</th>
<th>Kss</th>
</tr>
</thead>
<tbody>
<tr>
<td>AgClO₄</td>
<td>149</td>
<td>53</td>
<td>Ag₂SO₄</td>
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<td>0</td>
</tr>
<tr>
<td>AgBF₄</td>
<td>98</td>
<td>37</td>
<td>AgNO₃</td>
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<tr>
<td>CF₃SO₃Ag</td>
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<td>25</td>
<td>Ag₂CO₃</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AgPF₆</td>
<td>10</td>
<td>10</td>
<td>C₆H₅CO₂Ag</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CH₃SO₂Ag</td>
<td>0</td>
<td>0</td>
<td>CH₃CO₂Ag</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
The binding constants obtained for the \textit{ss} conformer (K\textsubscript{ss}) are also given in Table I. They are smaller than those of the \textit{aa} conformer. When clip 1b was titrated with AgClO\textsubscript{4} the conformational change only occurred to the \textit{aa} form. This suggests that the phenyl groups of clip 1a are involved in the binding process to the \textit{ss} conformer. The association constant for the complexation of AgClO\textsubscript{4} by the \textit{aa} conformer of 1b (K\textsubscript{aa} = 44 M\textsuperscript{-1}) is smaller than that by the \textit{aa} conformer of 1a (Table I). This is a result of the larger energy difference between the \textit{aa} and the \textit{sa} form of clip 1b\textsuperscript{4}. When no guest is present the amount of \textit{aa} conformer is almost zero, as can be concluded from \textsuperscript{1}H NMR experiments.

To locate the binding site of the silver ion, \textsuperscript{13}C-NMR experiments were carried out. \textsuperscript{13}C DEPT and 2-D HETCOR (HMOC) spectra were recorded to elucidate the complex \textsuperscript{13}C-NMR signals of clip 1a. Only the signals of the \textit{sa} conformer could be completely assigned. Those of the other conformers had intensities too low to give crosspeaks in the 2-D spectra. When AgClO\textsubscript{4} was added to a solution of 1a in CD\textsubscript{3}OD/CDC\textsubscript{13} (1:9, v/v), the aromatic region of the \textsuperscript{13}C spectrum changed considerably and became extremely complex. This suggests that the aromatic rings of 1 are involved in the process of complexation. In the region of the carbonyl and the methoxy groups no large shifts were observed, indicating that these groups are not involved in the binding.

To further determine the most favorable binding site for the silver ion, AM1 calculations were performed. The sites with the highest \(\pi\)-electron density can be expected to bind the silver ion. These are given in Figure 2a. A likely position of the silver ion is shown in Figure 2b.

\begin{center}
\textbf{Figure 2} The highest occupied \(\pi\)-orbitals according to AM1 calculations (a) and a likely place for binding of the silver ion to the \textit{aa} conformer of clip 1a (b).
\end{center}

The binding of a silver ion to the \textit{ss} conformer of clip 1a can occur at three places, viz. between the two phenyl rings, between a phenyl and a naphthalene ring, and on the top of one of the naphthalene walls (see Figure 3). Because the \textit{sa} conformer of 1b does not bind silver the last possibility is not likely. From
binding experiments with a diphenylglycol molecule without any walls we concluded that the silver ion is not bound between the phenyl groups. The most likely place for the silver ion, therefore, is between a naphthalene and a phenyl ring. Again, the most electron rich sites of the naphthalene moiety will be involved.

We are currently studying the allosteric binding properties of clip 1, i.e. the binding of aromatic guest molecules in the presence of Ag⁺ ions. Results will be presented in a full paper.

Figure 3. Schematic representation of the three possible binding places of the silver ion in the staggered conformation of la for the silver ion. The second place is the most likely one.

References

5. The compound was fully characterised by ¹H NMR, FAB-MS and elemental analysis.
6. Typical concentrations for 1 and for the silver salts are 2mM and 1 to 8-20 mM, respectively. The equations used to calculate the relative association constants are similar to those reported previously (see ref. 4). Analysis of the titration data revealed that only 1:1 complexes are formed.

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