π-π Interaction in the Complexes of the Pyridino-18-crown-6 Host Molecules and Aromatic Ammonium Salts as Determined by 1H NMR Spectroscopy

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Significant π-π interaction is found in the complexes of (S,S)-dimethylpyridino-18-crown-6 with (R)- and (S)-[α-(1-Naphthyl)ethyl]ammonium perchlorate. This finding is supported by the 1H NOESY NMR spectral technique, greater chemical shift changes of aromatic protons in both host and guest molecules upon complexation, and by molecular mechanics calculations.
TECHNICAL REPORT NO. 18

π-π Interaction in the Complexes of the Pyridino-18-crown-6 Host
Molecules and Aromatic Ammonium Salts as Determined by 1H NMR Spectroscopy

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March 19, 1993

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Enantiomeric recognition of chiral organic ammonium salts by many of these chiral macrocyclic ligands has been studied by NMR spectroscopy, calorimetric titration, solvent extraction, liquid membrane transport and chromatography. Detailed discussions of the synthesis and characterization of chiral ligands are given in a few reviews. Among the many chiral crown ethers, chiral pyridino-18-crown-6 ligands display moderate to significant recognition. However, interactions of most of the reported chiral ligands with enantiomeric guests have not been well characterized from either a thermodynamic or a kinetic standpoint. Structural and conformational studies of complexes in solution could provide evidence for the basis of enantiomeric recognition.

The primary binding force between the pyridino-crown ligand and the primary ammonium cation is that formed by the three hydrogen bonds as shown in Figure 1. However, the π–π interaction between the naphthene group of NapEt and the pyridine ring of the chiral ligand is considered as one of the possible causes for enantiomeric recognition. It is important to know if a π–π interaction exists and if it plays a role in promoting enantiomeric recognition in these chiral complexes. We now report an analysis of the π–π interaction in the complexes of (S,S)-Me,P18C6 with (R)- and (S)- NapEt in a 50%CD3OD and 50%CDCl3 (v/v) solvent system by 2D 1H NOESY spectroscopy and chemical shift changes.

**Experimental**

**NOESY Experiments:** 2D 1H NOESY spectra of (S,S)-Me,P18C6 complexes with (R)- and (S)-NapEt were taken on a Varian VXR-500 MHz NMR spectrometer at 25 °C. Stoichiometric amounts of host and guest were weighed on a high precision balance and dissolved in a mixed
solvent of 50%CD$_3$OD and 50%CDCl$_3$ (v/v) to give a concentration of 0.040 M. The 90 degree pulse width was always calibrated. Delay time was set to about 3 times the maximum T1 value.

Results and Discussion

When forming host-guest complexes with various ammonium salts in different solvent systems, the pyridine protons of the host showed significant chemical shift changes. A similar phenomenon has been observed in other systems. Table 1 lists the chemical shift values for free and complexed (S,S)-Me$_3$P$_{18}$C$_6$ with (R)-NapEt [(S,S)-(R)] and (S)-NapEt [(S,S)-(S)] as well as the differences between them. From these data, we can see that the pyridine proton in position 1 (Figure 1) has a 0.19 ppm upfield shift and a 0.01 ppm downfield shift in the of complexes with (R)-NapEt and (S)-NapEt, respectively. Proton 2 has 0.35 ppm and 0.10 ppm upfield shifts for (S,S)-(R) and (S,S)-(S) complexes, respectively. Significant changes (0.33 and 0.12 ppm upfield shifts) also occurred at position 4 which is close to the pyridine ring. Chemical shift changes can be caused by many factors such as hydrogen bonding, conformation changes, shielding and deshielding effects of aromatic rings, and π–π interactions. Hydrogen bonding and conformation changes should have little effect on the pyridine protons because the protons on the pyridine ring are not involved at the complexation site and the ring is a geometrically stable moiety. Deshielding and shielding effects of the π–π interacting units are thus expected to play an important role in the chemical shift changes of the pyridine protons. The chemical shift changes shown in Table 1 suggest the presence of a strong π–π interaction between the pyridine and naphthalene rings. This conclusion is supported by the chemical shift changes of guest molecule NapEt (Table 2).
chemical shift assignments were made from an $^1$H COSY spectrum. In this case, significant chemical shift changes occurred in positions A, C, E and F in the (S,S)-(R) complex and B, C and G in the (S,S)-(S) complex (see NapEt, Figure 1, for proton assignments). The relatively large chemical shift changes indicate that these positions are affected by the pyridine ring. The presence of positive and negative chemical shift changes results from shielding and deshielding effects of the pyridine ring depending on the relationship to the face or edge of the ring. Unlike a fixed structure in the crystalline state,$^{7,8}$ these data do not determine an absolute geometry for the interaction.

The data in Tables 1 and 2 also show that the protons in the (S,S)-(R) complex have a greater average chemical shift change than those in the (S,S)-(S) complex. Although the size of the absolute value of chemical shift change for a specific proton is not necessarily proportional to the stability of a complex,$^{10}$ the greater overall changes in the (S,S)-(R) complex over the (S,S)-(S) complex indicate greater stability for the (S,S)-(R) complex.

The presence of a $\pi-\pi$ interaction is also strongly supported by data from 2D $^1$H NOESY spectra (Figure 2). In the NOESY spectra, there are strong off-diagonal signals in the 7.2-8.2 ppm range between the chemical shifts of the pyridine and naphthalene protons indicating that pyridine protons of ligand and naphthalene protons of the ammonium salt are spatially close and that the complex is stable enough for NOE cross-relaxation to occur.$^{11}$ As shown in Figure 2, the $\pi$ systems overlap spatially in both the (S,S)-(R) (Figure 2a) and (S,S)-(S) (Figure 2b) complexes. This $\pi-\pi$ interaction helps bind the two aromatic systems together, determines the steric environment for the methyl groups, and contributes to recognition.
References


Table 1. $^1$H NMR Chemical Shift Values (ppm) for (S,S)-(S$_2$)P$_{18}$C$_6$ and Its Complexes with (R) & (S)-NapEt in 1M/1C* Mixed Solvent System (v/v) at 25°C

<table>
<thead>
<tr>
<th>Proton$^b$</th>
<th>(S,S)-Me$<em>2$P$</em>{18}$C$_6$ ppm</th>
<th>(S,S)-(R) Complex$^c$ ppm</th>
<th>(S,S)-(S) Complex$^d$ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.75</td>
<td>7.56</td>
<td>7.76</td>
</tr>
<tr>
<td>2</td>
<td>7.34</td>
<td>6.99</td>
<td>7.24</td>
</tr>
<tr>
<td>4</td>
<td>4.80</td>
<td>4.47</td>
<td>4.68</td>
</tr>
<tr>
<td>5</td>
<td>3.81</td>
<td>3.81</td>
<td>3.80</td>
</tr>
<tr>
<td>6</td>
<td>3.47</td>
<td>3.54</td>
<td>3.41</td>
</tr>
<tr>
<td>7&amp;8$^e$</td>
<td>3.59-3.48</td>
<td>3.78-3.68</td>
<td>3.62-3.48</td>
</tr>
<tr>
<td>9</td>
<td>1.19</td>
<td>1.25</td>
<td>1.18</td>
</tr>
</tbody>
</table>

$^a$M = CD$_3$OD, C = CDCl$_3$
$^b$Numbers correspond to protons in (S,S)-Me$_2$P$_{18}$C$_6$ (see structure)
$^c$(S,S)-(R) = Complex of (S,S)-Me$_2$P$_{18}$C$_6$ with (R)-NapEt
$^d$(S,S)-(S) = Complex of (S,S)-Me$_2$P$_{18}$C$_6$ with (S)-NapEt
$^e$Estimated values because of overlapping peaks.
Table 2. $^1$H NMR Chemical Shift Values (ppm) for (R) & (S) NapEt and Their Complexes with (S,S)-Me$_2$P18C6 in 1M/1C$^a$ Mixed Solvent System (v/v) at 25°C

<table>
<thead>
<tr>
<th>Proton</th>
<th>NapEt</th>
<th>(S,S)-(R) Complex$^c$</th>
<th>(S,S)-(S) Complex$^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ppm</td>
<td>ppm</td>
<td>Δppm</td>
</tr>
<tr>
<td>A</td>
<td>7.63</td>
<td>7.78</td>
<td>+0.15</td>
</tr>
<tr>
<td>B</td>
<td>7.65</td>
<td>7.61</td>
<td>-0.04</td>
</tr>
<tr>
<td>C</td>
<td>8.07</td>
<td>7.94</td>
<td>-0.13</td>
</tr>
<tr>
<td>D</td>
<td>7.92</td>
<td>7.84</td>
<td>-0.08</td>
</tr>
<tr>
<td>E or F</td>
<td>7.59</td>
<td>7.25</td>
<td>-0.34</td>
</tr>
<tr>
<td>F or E</td>
<td>7.59</td>
<td>7.40</td>
<td>-0.19</td>
</tr>
<tr>
<td>G</td>
<td>7.94</td>
<td>7.84</td>
<td>-0.10</td>
</tr>
<tr>
<td>K</td>
<td>5.34</td>
<td>5.35</td>
<td>+0.01</td>
</tr>
<tr>
<td>L</td>
<td>1.79</td>
<td>1.84</td>
<td>+0.05</td>
</tr>
</tbody>
</table>

$^a$ See footnote a in Table 1
$^b$ Letters correspond to protons in NapEt (see structure)
$^c$ See footnote c in Table 1
$^d$ See footnote d in Table 1
Figure 2. $^1$H NMR NOESY spectra of complexes of (S,S)-dimethylpyridino-18-crown-6 with (R)-[$\alpha$-(1-Naphthyl)ethyl]ammonium perchlorate (Figure 2a) and (S)-perchlorate (Figure 2b) in a mixed solvent of 50%CD$_3$OD + 50%CDCl$_3$, at 25°C.
Figure 1. Structures of Compounds

Me$_2$P18C6

NapEt

Tripoa