Cation-Binding Hosts

Classes of cyclic and acyclic ligands

- Open chain
- Cyclic
- Three-dimensional

Podand
D = donor atom

Corand
D = O, Crown ether

Cryptand
B = bridgehead atom
• Podands

• Corands

Crown ethers
Azacorands

- 18<N_62_6>corand-6
- [18]ane-N_6 hexacyclen
- 14<N_42_3_2>corand-4
tetraza[14]crown-4 cyclam
- 18<O_3N_32_6>corand-6

Azacorands

• Lariat ethers (corand-podand hybrids)

BiBLE (bi-bracchial lariat ether)
- Cryptands

Crypt from the Latin *crypta*, meaning concealed, private
• **Crown Ethers**

Accidental synthesis of the first crown ether, dibenzo[18]crown-6, by Pedersen

\[
\text{Minor product} \\
\begin{align*}
\text{trace amount (contaminant)} \\
\text{Major product}
\end{align*}
\]

**Cyclic Polyethers and Their Complexes with Metal Salts**

C. J. Pedersen

*Contribution No. 157 from E. I. du Pont de Nemours and Company, Inc., Elastomer Chemicals Department, Experimental Station, Wilmington, Delaware 19898. Received April 13, 1967*

*JACS, 1967, 89, 7017*
Common crown ethers

Complementary to Na⁺

[18]crown-6
Complementary to K⁺

[21]crown-7
Complementary to Cs⁺

Dicyclohexyl[18]crown-6
More conformationally rigid

Dibenzo[30]crown-10
Binds two Na⁺ ions

Dibenzo[26]crown-4
An unusual example

Space-filling model of complex between 18-C-6 and K⁺
Table 1. Binding Data for Simple Crown Ethers

<table>
<thead>
<tr>
<th>compound</th>
<th>solvent</th>
<th>dielectric, $\epsilon$</th>
<th>log $K_S$ Na$^+$</th>
<th>log $K_S$ K$^+$</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-crown-4</td>
<td>methanol</td>
<td>33</td>
<td>1.7</td>
<td>1.3</td>
</tr>
<tr>
<td>15-crown-5</td>
<td>methanol</td>
<td>33</td>
<td>3.24</td>
<td>3.43</td>
</tr>
<tr>
<td>18-crown-6</td>
<td>dioxane</td>
<td>2</td>
<td>4.55</td>
<td></td>
</tr>
<tr>
<td>18-crown-6</td>
<td>methanol</td>
<td>33</td>
<td>4.35</td>
<td>6.08</td>
</tr>
<tr>
<td>18-crown-6</td>
<td>acetonitrile</td>
<td>37</td>
<td>4.8</td>
<td>5.7</td>
</tr>
<tr>
<td>18-crown-6</td>
<td>water</td>
<td>80</td>
<td>1.8</td>
<td>2.06</td>
</tr>
</tbody>
</table>

Figure 15. Binding constants (log $K_S$) for $3n$-crown-$n$ ($n = 4$–$8$) compounds with Na$^+$, K$^+$, Ca$^{2+}$, and NH$_4^+$ determined in CH$_3$OH at 25 $^\circ$C.
Table 2.1  Binding constants obtained for various cations and a selection of crown ethers (log $K$, methanol, 20°C)

<table>
<thead>
<tr>
<th>Crown ether</th>
<th>Na$^+$</th>
<th>K$^+$</th>
<th>Rb$^+$</th>
<th>Cs$^+$</th>
<th>Ca$^{2+}$</th>
<th>NH$_4^+$</th>
</tr>
</thead>
<tbody>
<tr>
<td>[12]crown-4</td>
<td>1.70</td>
<td>1.30</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>[15]crown-5</td>
<td>3.24</td>
<td>3.43</td>
<td>—</td>
<td>2.18</td>
<td>2.36</td>
<td>3.03</td>
</tr>
<tr>
<td>[18]crown-6</td>
<td>4.35</td>
<td>6.08</td>
<td>5.32</td>
<td>4.70</td>
<td>3.90</td>
<td>4.14</td>
</tr>
<tr>
<td>[21]crown-7</td>
<td>2.52</td>
<td>2.35</td>
<td>—</td>
<td>5.02</td>
<td>2.80</td>
<td>3.27</td>
</tr>
<tr>
<td>Benzo[18]crown-6</td>
<td>4.30</td>
<td>5.30</td>
<td>4.62</td>
<td>3.66</td>
<td>3.50</td>
<td>—</td>
</tr>
</tbody>
</table>

X-ray crystal structures of [18]crown-6 containing (a) Na$^+$, (b) K$^+$, (c) Cs$^+$ and (d) two Li$^+$ ions (phenolate salt). Na–O bond lengths are significantly longer than optimal.
Methods for synthesizing the crown ethers \((R - V\) are organic linker groups).
The term **podand** was coined by Vögtle and Weber in 1979, referring to acyclic hosts with pendant binding sites, *e.g.*

Podand hosts generally exhibit less cation affinity than their cyclic analogues, as a result of their lack of **preorganisation**, but they may adopt similar wrapping conformations to the crown ethers in the presence of suitable metal cations.

X-ray molecular structure of the europium(III) podand complex 
\[ [\text{Eu(H}_2\text{O})_3(3.12)]^{3+} \]
Endgroup Concept

Compared to crown ethers, podands show higher degree of flexibility, allowing them to adopt non-binding open conformations. If the podand is terminated by a rigid functionality (e.g. aryl, ester, amide), however, binding is enhanced by the extra degree of organization given to the podand host by the rigidifying endgroup.
The term **lariat ether** (from Spanish *la reata*, lasso) refers to a crown ether or similar macrocyclic derivative with one or more accompanying appendages designed to enhance metal cation complexation ability by giving some three-dimensionality to the binding, e.g.
Examples of lariat ether synthesis

\[
\text{O} - \text{Me} \xrightarrow{\text{TsCl, pyridine, } 0^\circ\text{C, 10 min}} \text{TsO} - \text{Me}
\]
\(\text{Ts} = \text{O}_2\text{S}C_6\text{H}_4\text{Me}\)

(a)

\[
\text{H-} - \text{N-} \xrightarrow{\text{MeO, Na}_2\text{CO}_3} \text{N} - \text{OH} \xrightarrow{\text{NaH / dmf}} \text{Tso(CH}_2\text{CH}_2\text{O})_4\text{Ts}
\]

(b)

\[
\text{Br-} \xrightarrow{\text{ROH}} \text{RO-} \xrightarrow{\text{BrNHCOMe}} \text{HO(CH}_2\text{CH}_2\text{O})_4\text{H}
\]

3.20 \(R = \alpha\text{-C}_6\text{H}_4\text{OMe}\)

3.21 \(R = \rho\text{-C}_6\text{H}_4\text{OMe}\)
Simultaneous four-bond coupling to produce BiBLE ligands

\[
\begin{align*}
\begin{array}{ccc}
R \text{NH}_2 & + & \begin{array}{c}
\text{I} \\
\text{I} \\
\text{O} \\
\text{O} \\
\text{O} \\
\text{I} \\
\text{I}
\end{array} \\
\text{MeCN} & \xrightarrow{\text{Na}_2\text{CO}_3} & \begin{array}{c}
\text{R} \\
\text{N} \\
\text{O} \\
\text{O} \\
\text{O} \\
\text{O} \\
\text{O} \\
\text{R}
\end{array}
\end{array}
\end{align*}
\]

\[
R = \begin{array}{c}
\text{cyclohexane} \\
\text{cyclohexyl} \text{OMe} \\
\text{pyrrolidine} \\
\text{acetylene} \\
\text{furan}
\end{array}
\]

(* = point of attachment)
A lariat ether-based flouremetric sensor

Log $K$ (M$^{-1}$)

<table>
<thead>
<tr>
<th>Ion</th>
<th>Log $K$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca$^{2+}$</td>
<td>7.6</td>
</tr>
<tr>
<td>Sr$^{2+}$</td>
<td>6.8</td>
</tr>
<tr>
<td>Ba$^{2+}$</td>
<td>6.9</td>
</tr>
</tbody>
</table>

Measured in CH$_3$CN/CHCl$_3$ (99:1) (1:1 binding)

Crown ethers in molecular devices

- A spirobenzopyran-based crown ether for ion sensing

- A saxitoxin sensor

- A luminescent sensor for ion pairs
• A molecular “AND” logic gate

• Viologen-rotaxane switches
• A molecular elevator

• A molecular motor with a self-complexing lock

Feringa, *Angew. Chem.* 2010, asap article