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quenched with a solution of citric acid. The mixture was diluted with DCM (100 mL) and washed with sodium bicarbonate (saturated), water, and brine (25 mL each). The organic layer was dried (Na$_2$SO$_4$), evaporated, and re-disolved in DCM (0.65 mg, 55%)

To 4 (4.6 mg, 0.002 mmol) in THF/water (10:1, 200 pL), DBU (3 pL) and 0.1 % TFA/MeCN 70/30 -» 10/90 in 30 min. 70 °C) to afford the pure cyclic peptide acid (30 pL), the DCM evaporated, and the residue dissolved in acetonitrile and (1.2 mL) was stirred for 48 h at RT. The reaction mixture was quenched with acetic acid (20 pL) and purified by reverse-phase HPLC (Beckman ODS ultrasphere pool of silica gel, EtOAc/acetone 9:1) to afford 4 (19 mg, 80%).

To 2 (46.6 mg, 0.002 mmol) in THF/water (10:1, 200 pL), DBU (3 pL) and lithium bromide (2 mg) were added. After stirring overnight at RT, DCM (4 pL) and lithium bromide (3 mg) were added again. After 5 h, the reaction was quenched with acetic acid (20 pL) and purified by reverse-phase HPLC (Beckman ODS ultrasiexphere 5 x 10 mm x 25 mm, 0.1 % TFA/McCN 70/30 -10/90 in 30 min, 30 °C, 3 runs) to yield the peptide precursor of 5 (0.2 mg, 60%). A solution of this peptide precursor (1.2 mg, 0.007 mmol) and 2,6-lutidine (4 pL) in DCM (15 mL) was stirred for 1 h at 0 °C and allowed to warm to RT overnight. The mixture was diluted with DCM (50 mL) and washed three times with sodium bicarbonate (sat.), water, sodium bicarbonate (saturated), water, and brine (30 mL each). The organic layer was dried (Na$_2$SO$_4$), evaporated, and re-disolved in DCM (30 mL). Fmoc-N-Melle (12 mg, 0.032 mmol), PyBroP (14 mg, 0.032 mmol) and DIPEA (300 pL) were added at 0 °C. After 2 h at 0 °C the reaction was allowed to warm to RT, diluted with DCM (50 mL), washed with sodium bicarbonate (1 %), water, sodium bicarbonate (saturated), water, and brine (30 mL each). The organic layer was dried (Na$_2$SO$_4$), evaporated, and chromatographed (silica gel, EtOAc/acetone 9:1) to afford 5 (16 mg, 80%).

To 3 (27 mg, 0.022 mmol) in DCM (1 mL), TFA (0.5 mL) was added dropwise at 0 °C and allowed to warm to RT overnight. The mixture was diluted with DCM (50 mL) and washed three times with sodium bicarbonate (sat.), water, sodium bicarbonate (saturated), water, and brine (30 mL each). The organic layer was dried (Na$_2$SO$_4$), evaporated, and re-disolved in MeOH/water (10:1, 200 pL), DBU (3 pL) and 0.1 % TFA/MeCN 70/30 -» 10/90 in 30 min. 70 °C) to afford the pure cyclic peptide acid (18 pL), the DCM evaporated, and the residue dissolved in acetonitrile and (1.2 mL) was stirred for 48 h at RT. The reaction mixture was quenched with acetic acid (20 pL) and purified by reverse-phase HPLC (Beckman ODS ultrasphere pool of silica gel, EtOAc/acetone 9:1) to afford 6 (19 mg, 50%).

To 4: To 3 (27 mg, 0.022 mmol) in DCM (1 mL), TFA (0.5 mL) was added dropwise at 0 °C and allowed to warm to RT overnight. The mixture was diluted with DCM (50 mL) and washed three times with sodium bicarbonate (sat.), water, sodium bicarbonate (saturated), water, and brine (30 mL each). The organic layer was dried (Na$_2$SO$_4$), evaporated, and re-disolved in MeOH/water (10:1, 200 pL), DBU (3 pL) and 0.1 % TFA/MeCN 70/30 -» 10/90 in 30 min. 70 °C) to afford the pure cyclic peptide acid (18 pL), the DCM evaporated, and the residue dissolved in acetonitrile and (1.2 mL) was stirred for 48 h at RT. The reaction mixture was quenched with acetic acid (20 pL) and purified by reverse-phase HPLC (Beckman ODS ultrasiexphere 5 x 10 mm x 25 cm, 0.1 % TFA/McCN 70/30 -10/90 in 30 min, 70 °C) to afford the pure cyclic peptide 5 (0.65 mg, 55%).

Keywords: cyclophilin - cyclosporin - immunophilins - protein dimerization


Strong Binding of Parauat and Polymeric Parauat Derivatives by Basket-Shaped Hosts**

Albertus P. H. J. Schenning, Bas de Bruin, Alan E. Rowan,* Huub Kooijman, Anthony L. Spek, and Roeland J. M. Nolte

Clip-shaped host molecules of type 1 can bind uncharged aromatic guest molecules, for example resorcinol, by n–π stacking and hydrogen bonding interactions.[1] Basket-shaped deriva­tives of 1 containing crown ether moieties (compounds of type 2) are, in addition, able to bind alkalai metal ions and protonated amines.[2] We report here on the binding affinities of these host molecules towards charged aromatic compounds, such as paraquat 3 and the polymeric paraquat derivatives 4 and 5.

5. There is currently a great deal of interest in paraquat-binding, which has resulted in the design and construction of new molecular structures, as exemplified by the elegant work by Stoddart et al. on catenands and rotaxanes.[3] We describe here that com­pounds 5 and 6.

[*] Dr. A. E. Rowan, Dipl-Chem. A. P. H. J. Schenning, Dipl-Chem. D. de Bruin, Prof. Dr. R. J. M. Nolte

**Department of Organic Chemistry, NSR Center

University of Nijmegen

Toernooiveld, NL-6525 ED Nijmegen (The Netherlands)

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is not tilted. The binding constant of the bis(paraphenylene)-
[34]crown-10 macrocycle with 3-(PF$_6$)$_2$ in acetone is 730 m$^{-1}$. The binding properties of 1 and 2 were evaluated by recording the intensity of the charge-transfer absorption band at approximately 425 nm at different host–guest ratios. The results for different solvents are presented in Table 1. The basket-shaped host molecules 2 bind paraquat approximately 25–75 times stronger than the bis(paraphenylene)-[34]crown-10 macrocycle. This result can be explained from the fact that compounds 2 are more preorganized for binding than Stoddart’s compound. Only a very small $K_c$ of 80 m$^{-1}$ was found for the binding of 3 in the cavity of clip molecule 1. This clearly demonstrates the importance of the crown ether moieties in 2 for the complexation of paraquat.

**Table 1. Binding constants (a) of the complexes between hosts 1 and 2 and guests 3, 4, and 5**

<table>
<thead>
<tr>
<th>Host</th>
<th>Guest</th>
<th>$K_c$, m$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3-Cl$_2$</td>
<td>50 [h]</td>
</tr>
<tr>
<td>2a</td>
<td>3-(PF$_6$)$_2$</td>
<td>57000 [c]</td>
</tr>
<tr>
<td>2a</td>
<td>4-(PF$_6$)$_2$</td>
<td>20600 [d]</td>
</tr>
<tr>
<td>2b</td>
<td>3-Cl$_2$</td>
<td>22000 [f]</td>
</tr>
<tr>
<td>2a</td>
<td>4a (f)</td>
<td>1800 [c, e]</td>
</tr>
<tr>
<td>2a</td>
<td>4b (g)</td>
<td>4500 [c, e]</td>
</tr>
<tr>
<td>2a</td>
<td>5a (h)</td>
<td>19000 [c, e]</td>
</tr>
</tbody>
</table>

[a] Association constants were calculated using the Benesi–Hildebrand equation [13]. Good correlations ($R > 0.995$) were obtained for all titration curves assuming a 1:1 host–guest complexation. Estimated error in $K_c$ is 10%. For the $K_c$ measured in acetonitrile, the error is 50% due to the poor solubility of the host molecule in this solvent. [b] Methanol-chloroform (1:1, v/v). [c] Acetonitrile. [d] Acetonitrile, 25°C. [e] Intrinsic viscosity of polymer [η] = 0.066 dl·g$^{-1}$ (acetonitrile, 25°C). [f] Intrinsic viscosity of polymer [η] = 0.20 dl·g$^{-1}$ (acetonitrile, 25°C). [g] Average degree of polymerization $= 4$ (NMR, endgroup analysis).

The electrochemical behavior of the complex between 3-(PF$_6$)$_2$ and compound 2a was studied in acetonitrile. In this solvent the guest showed two reversible one-electron transfers: $E_{1/2}(2+/+1) = -0.423$ V, $E_{1/2}(1+/0) = -0.840$ V (vs. SCE, for both transitions $\Delta E_p = 60$ mV). Upon the addition of one equivalent of 2a the first redox transfer shifted 100 mV to more negative potential, whereas the second electron transfer potential remained unaffected. These data indicate that 2a binds and stabilizes the doubly charged paraquat species, which results in a more negative redox potential for the first redox transfer. It is well known that in this type of host–guest system the guest reduced by one electron dissociates from the host, and this explains the unaltered second redox potential.

PolymERIC paraquat derivatives have previously been investigated as redox-active films and more recently as optical data storage materials and show a wide variety of electrochromic and thermochromic behavior [4, 9, 10]. The polymeric paraquat derivative with tosylate counterions has been shown to possess liquid crystalline properties [11, 12]. We felt that host–guest complexation might be an interesting way to modify and control the physical properties of this interesting class of polymers. The results of binding studies carried out in acetonitrile, showed that 2a can be clipped to polymeric paraquat derivatives 4a, 4b, and 5 with association constants of 1800 m$^{-1}$, 4500 m$^{-1}$, and 19000 m$^{-1}$, respectively (per polymer repeat unit, see Table 1, Fig. 1). The binding constants of 4a and 4b are lower than those observed for paraquat itself. Molecular modeling studies have revealed that in the case of 4a and 4b, complexation of a basket to a paraquat unit in the polymer is sterically hindered by baskets complexed to adjacent paraquat units. The overall lower binding constants reflect this steric hindrance, which is less for
the polymer with a longer spacer (4b) than for the one with the smaller spacer (4a). Viscosity measurements showed that the specific viscosity of the polymers solubilized in acetonitrile increases upon the addition of 0.03 equivalents of the host molecule 2a per repeat unit: for example, 4a: \( \eta_{sp} = 0.006, Aa = 2a \eta_{sp} = 0.008; 4b: \eta_{sp} = 0.068, Bb = 2a \eta_{sp} = 0.070 \). These results indicate that the average molecular mass of the polymers increases on complexation with 2a. The redox potentials of the polymers were also influenced by the hosts. Polymer 4a displayed the following redox transitions in acetonitrile: 

\[ E_{1/2}(2a/1+) = -0.387 \text{V}, E_{1/2}(1+/0) = -0.840 \text{V} \text{ vs. SCE, for both transitions } \Delta E = 60 \text{ mV}. \]

Values are smaller than the 100 mV shift measured for paraquat ket molecules. This may be of interest for future application of these polymers as optical data storage systems or as molecular switches, etc.

In conclusion, we have shown that host molecules of the type 2 strongly bind paraquat 3 and that it is possible to clip these molecules to polymeric paraquat derivatives. Further studies are underway.

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**Keywords:** crown ethers • paraquat • supramolecular chemistry

**COMMUNICATIONS**

**Formation of a "meso-Helicate" by Self-Assembly of Three Bis(catecholate) Ligands and Two Titanium(IV) Ions**

Markus Albrecht* and Siripol Kotila

Double- or triple-helical oligomerculear coordination compounds that are formed spontaneously by self-assembly of two or three oligofunctional ligands and several metal ions are called helicates. Due to their helicity, such molecules are chiral. On the other hand, meso-helicates are analogous metal complexes with two differently configurated helical units and are thus achiral. In a topological sense, the meso-helicates are helices that inverse their helical twist.

An octahedral complex formed by one metal center and two bidentate ligands is the most simple helical unit. It has two configurations (A and A'). Double bridging between the ligands of two such octahedrons results in the formation of three different coordination compounds: the enantiomeric A,A- and A,A-helicates, and the diasteromeric A,A-form—the most simple triple-stranded meso-helicate (Fig. 1).

The coordination chemistry of linear oligofunctional nitrogen donor ligands with soft metal ions has recently become the focus of a great deal of attention. To our knowledge, investigations towards the metal-directed self-assembly of helicates have resulted only in the characterization of double- and triple-helicates and double-stranded non-helical metal complexes, which do not possess units with helical chirality.

In this context, the triple-stranded meso-helicate is a missing structural motif. This stimulated our interest in self-assembly processes based on oxygen donor ligands in combination with hard metal ions. The use of early transition metals should provide access to new supramolecular aggregates, whose properties should differ from those of the "traditional" compounds. Catechol ligands seem to be ideal bidentate chelating units for this purpose. Initially we chose the (CH₂)₃ group as a spacer.

**[**] Dr. M. Albrecht  
Institut für Organische Chemie der Universität  
Richard-Wagner-Allee, D-76131 Karlsruhe (Germany)  
Tel.: Fax: Int. code +49 (721) 608829  
Dr. S. Kotila  
Organisch-Chemisches Institut der Universität Münster (Germany)

**[**] This work was supported by the Fonds der Chemischen Industrie (Liebig Stipendium), the Deutsche Forschungsgemeinschaft, and the Academy of Finnland. Dr. H. Röttele is thanked for the NMR measurements, Mrs. B. Wübbeling's and Dr. R. Feldhütter's help with the X-ray structure analysis is gratefully acknowledged.

Fig. 1. Schematic representation of a) a helicate (here: A-A-form) and the corresponding meso-helicate (A-A-A-form) and b) a bidentate CH₂-bridged helicate and meso-helicate (only one of the ligand strands is shown).


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**[**] Dr. M. Albrecht  
Institut für Organische Chemie der Universität  
Richard-Wagner-Allee, D-76131 Karlsruhe (Germany)  
Tel.: Fax: Int. code +49 (721) 608829  
Dr. S. Kotila  
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