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COMMUNICATIONS

quenched with a solution of citric acid. The mixture was diluted with DCM (100 mL) and washed with sodium bicarbonate (sat.), water, and brine (25 mL each). The organic layer was dried (Na2SO4), evaporated, and the residue was dissolved in DCM/MeOH (98:2) and filtered through a plug of silica gel. Evaporation gave the crude precursor of 2 (773 mg). To this crude product (746 mg) in DCM (100 mL), washed with sodium bicarbonate (sat.), water, and brine (25 mL each). The organic layer was dried (Na2SO4), evaporated, and redissolved in DCM (0.5 mL). Boc-(2S,3R,4S,5R,6S)-3-carboxy-4-methyl-2-(methylamino)-6-octenoic acid (Boc-HeX) (27 mg, 0.060 mmol) and DIFPE (27 μL) were added and the mixture was stirred for 1 h at 0°C, diluted with DCM (50 mL), washed with sodium bicarbonate (sat.), water, sodium bicarbonate (sat.), water, and brine (20 mL each). The organic layer was dried (Na2SO4), filtered, evaporated, and chromatographed (silica gel, EtOAc/EtOH 9:1) to afford 4 (19 mg, 60%).

5: To 4 (4.6 mg, 0.0028 mmol) in THF/water (10:1, 200 μL), DIBU (3 μL) and lithium bromide (2 mg) were added. After stirring overnight at RT, DIBU (4 μL) and lithium bromide (3 mg) were added again. After 5 h, the reaction was quenched with acetic acid (20 μL) and purified by reverse-phase HPLC (Beckman ODS ultrapure 5 μm 10 mm × 25 mm, 0.1% TFA/MeCN 70:30 to 10:90 in 30 min, 70°C, 3 runs) to yield the peptide precursor of 5 (0.2 mg, 60%). A solution of this peptide precursor (2.1 mg, 60%), A solution of this peptide precursor (1.2 mg, 970 nmol), AOP[17] (4 mg, 0.009 mmol) and 2,6-lutidine (4 μL) in DCM (15 μL) were added and the mixture was stirred for 6 h at 0°C and 30 min at RT. Fmoc-N-Mel (5 mg, 0.013 mmol), PyBroP (5 mg, 0.011 mmol) were added again and the mixture was stirred for 1 h at 0°C, diluted with DCM (50 mL) and washed three times with sodium bicarbonate (sat.), water, and brine (10 mL each). The organic layer was dried (Na2SO4), filtered and evaporated. To the residue in DCM (30 μL), Boc-(2S,3R,4S,5R,6S)-3-carboxy-4-methyl-2-(methylamino)-6-octenoic acid (Boc-HeX) (27 mg, 0.060 mmol) and DIFPE (27 μL) were added and the mixture was stirred for 6 h at 0°C and 30 min at RT. After 2 h at 0°C the solution was diluted to RT, diluted with DCM (50 mL), washed with sodium bicarbonate (sat.), water, sodium bicarbonate (sat.), water, and brine (20 mL each). The organic layer was dried (Na2SO4), evaporated, and chromatographed (silica gel, EtOAc/EtOH 9:1) to afford 4 (19 mg, 60%).

Strong Binding of Paraquat and Polymeric Paraquat 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. Basket-shaped derivatives of 1 containing crown ether moieties (compounds of type 2) are, in addition, able to bind alkali metal ions and protonated amines. 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. 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. We describe here that compound 5.

Keywords: cyclophilin - cyclosporin - immunophilins - protein dimerization


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Compound 2 is an exceptionally good host for paraquat. This opens
the possibility of clipping host molecules of type 2 to polymeric
chains containing paraquat units. The X-ray structure and
properties of the complex between 2 and paraquat are also pre-
sented.

Compounds 1 and 2 were synthesized as described previously.[1,2] For the synthesis of 2b, 4,4'-dimethyldenediphenyl was used as
the starting material. Compounds 3 and 4 were prepared by
using literature procedures.[3,4] Compound 5 was prepared by
the condensation of N,N'-bis-(2-hydroxyethyl)-4,4'-bipyrinidini-
um hexafluorphosphate in acetonitrile with one equivalent of
diethyl chloride with triethylamine as the base,[3] and purified
by precipitation from ethyl acetate.

Addition of 3-Cl2 to a solution of host 2b in for example
methanol/chloroform led to an immediate color change from
coloreless to yellow-orange, indicative of the formation of a
charge-transfer complex.[5]1 H NMR spectroscopic studies re-
vealed that in this complex the paraquat guest is located in the
cleft of the cavity.[6] Fast atom bombardment mass spectrome-
try (FAB MS) showed a peak at m/z 1094 (matrix: nitrobenzyl
alcohol), which corresponds to the mass of the host–guest com-
plex. Crystals of the complex between 2b and 3-[PF6]2, suitable
for X-ray analysis were grown from a mixture of 2b and tetra-
butylammonium hexafluorophosphate dissolved in chloroform,
which was layered with 3-Cl2 in methanol. The X-ray structure
of complex is shown in Figure 1 (top).[7] It reveals a

Perfect complementarity between host and guest. The paraquat
guest sits symmetrically within the walls of the basket; the
methyl substituents are partially encapsulated by the crown
ether rings. The crystal structure is different from that of the
complex of paraquat with "bis(paraphenylene)-[34]crown-10" (the
same macrocycle as compound 2a, but without the
diphenylglycoluril unit), as published by Stoddart et al.[8] In
the case of the latter the bipyridinium guest is flat, whereas in
the crystal structure described herein the two bipyridinium units
are twisted by an angle of 22.5°. This is a consequence of being
less sterically constrained by the aromatic side walls of the
basket. In Stoddart's compound the bipyridinium is tilted at
an angle of about 28° with respect to the O–O axis of the para-
phenylene unit; in our case the bipyridinium guest in the basket
is not tilted. The binding constant of the bis(paraphenylene)-
[34]crown-10 macrocycle with 3-[PF6]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 approxi-
mately 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 macro-
cycle.[9] This result can be explained from the fact that com-
 pounds 2 are more preorganized for binding than Stoddart's
compound.[10] Only a very small $K_g$ of 80 m-1 was found for the
binding of 3 in the cavity of clip molecule 1. This clearly dem-
onstrates the importance of the crown ether moieties in 2 for
the complexation of paraquat.

<table>
<thead>
<tr>
<th>Host</th>
<th>Guest</th>
<th>$K_g$ [M-1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3-Cl2</td>
<td>60 [b]</td>
</tr>
<tr>
<td>2a</td>
<td>3-[PF6]2</td>
<td>57000 [c]</td>
</tr>
<tr>
<td>2a</td>
<td>4-[PF6]2</td>
<td>80000 [d]</td>
</tr>
<tr>
<td>2b</td>
<td>3-Cl2</td>
<td>22000 [b]</td>
</tr>
<tr>
<td>2a</td>
<td>4-[PF6]2</td>
<td>1800 [c, e]</td>
</tr>
<tr>
<td>2a</td>
<td>3-[PF6]2</td>
<td>4500 [c, e]</td>
</tr>
<tr>
<td>2a</td>
<td>5-[PF6]2</td>
<td>19000 [c, e]</td>
</tr>
</tbody>
</table>

[b] Association constants were calculated using the Benesi–Hildebrand equation
[c] Good correlations ($R > 0.995$) were obtained for all titration curves assuming
[d] Per polymer repeat unit. [f] Intrinsic viscosity of polymer [g] = 0.0066 dl·g-1 (acetonit-
C. We felt that [j] Average degree of polymerization = 4 (NMR, endgroup analysis).

The electrochemical behavior of the complex between 3-
([PF6]2 and compound 2a was studied in acetonitrile. In this
solvent the guest showed two reversible one-electron transfers:
$E_{1/2}^{o}(2+/1+) = -0.423$ V, $E_{1/2}^{o}(1+/0) = -0.840$ V (vs. SCE,
for both transitions $E_{1/2} = 60$ 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 poten-
tial 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 host
reduced by one electron dissociates form the host, and this ex-
plains the unaltered second redox potential.[11]

Polymere paraquat derivatives have previously been investi-
gated as redox-active films and more recently as optical data
storage materials and show a wide variety of electrochromic
and thermochromic behavior.[12,9,10] The polymeric paraquat
derivative with tosylate counterions has been shown to possess
liquid crystalline properties.[11]1 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 derivates 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 bask-
ets complexed to adjacent paraquat units. The overall lower
binding constants result from steric hindrance, which is less for

Fig. 1. Top: Crystal structure of the complex between 2b and 3-[PF6]2. Left top
view, right side view [14]. Bottom: Computer-generated model of the complex
between 2b and 5.
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: ηsp = 0.006, 4a + 2a ηsp = 0.008; 4b: ηsp = 0.068, 4b + 2a ηsp = 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: 

$$E_{1/2}(2+/+1) = -0.387 \text{ V, } E_{1/2}(+1/0) = -0.840 \text{ V (vs. SCE, for both transitions } \Delta E = 60 \text{ mV). Upon the addition of one equivalent of } 2a \text{ per repeat unit the first redox transfer shifted 20 mV to more negative potential, whereas the second redox transfer remained unchanged. }$$

Addition of three equivalents of 2a resulted in a 35 mV shift in the negative direction. These shift values are smaller than the 100 mV shift measured for paraquat 

$$EU2(2+/i+) = -0.387 \text{ V, } EU2(2+/i+) = -0.387 \text{ V, }$$

displayed the following redox transitions in acetonitrile: 

$$Ep(2+/i+) = -0.270 \text{ V, } Ep(2+/i+) = -0.270 \text{ V, }$$

indicate that the average molecular mass of the polymers increases upon the addition of 0.03 equivalents of the host molecule 2a per repeat unit: for example, 4a:

$$\mu = 1.08 \text{ (d, 4H, Ar-H), } +0.12 \text{ (d, 6H, CH_3).}$$

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.

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

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**COMMUNICATIONS**

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

Markus Albrecht* and Sirpa Kotila

Double- or triple-helical oligomeric coordination compounds that are formed spontaneously by self-assembly of two or three oligofoligand ligands and several metal ions are called helicates. Due to their helicity, such molecules are chiral.16 On the other hand, meso-helicates are analogous metal complexes with two differently configured helical units and are thus achiral. In a topological sense, the meso-helicates are helices that inverse their helical twist.17

An octahedral complex formed by one metal center and three bidentate ligands is the most simple helical unit. It can have two configurations (A or A').18 Triple 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 diastereomeric A,A-form—the most simple triple-stranded meso-helicate (Fig. 1).

The coordination chemistry of linear oligofoligand 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-11,41 and triple-helicate15 and double-stranded non-helical metal complexes, which do not possess units with helical chirality.16

In this context, the triple-stranded meso-helicate is a missing structural motif. This stimulated our interest in self-assemble processes based on oxygen donor ligands in combination with hard metal ions17,18. 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.10 Initially we chose the (CH_3)_2 group as a spacer.

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**Fig. 1. Schematic representation of a) a helicate (here: A,A-form) and the corresponding meso-helicate (A,A,A-form) and b) a bistraded C_2-bridged helicate and meso-helicate (only one of the ligand strands is shown).**

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**[**] Dr. M. Albrecht**