

Bipyridine functionalized molecular clips. Self-assembly of their ruthenium complexes in water

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Ruthenium-bipyridine complexes of molecular clips self-assemble in water to form scroll- and cigar-like nanostructures.

The development of artificial self-assembled structures with specific shape and size is a topic of fundamental importance.^{1,2} Incorporation of metal centers into these structures is of great interest as it may eventually lead to functional nanosized devices, for which many applications can be foreseen.

In our work to construct well defined nanosized assemblies by means of molecular recognition, we recently reported the formation of 'razorblade-like' aggregates in water, which were built up from diphenylglycoluril (DPG) derived molecular clips with water-soluble groups on their convex side.³ Dimerization of these clips, in which the cavity of one clip is filled by the sidewall of its neighbour and *vice versa*, was found to play a major role in the assembly process. In order to be able to incorporate metal centers in these assemblies, a new type of molecular clip was developed having a bipyridine ligand on its convex side. Here the synthesis and properties of two of these clips are presented, as well as the self-assembling behaviour of their ruthenium-bipyridine complexes in water.

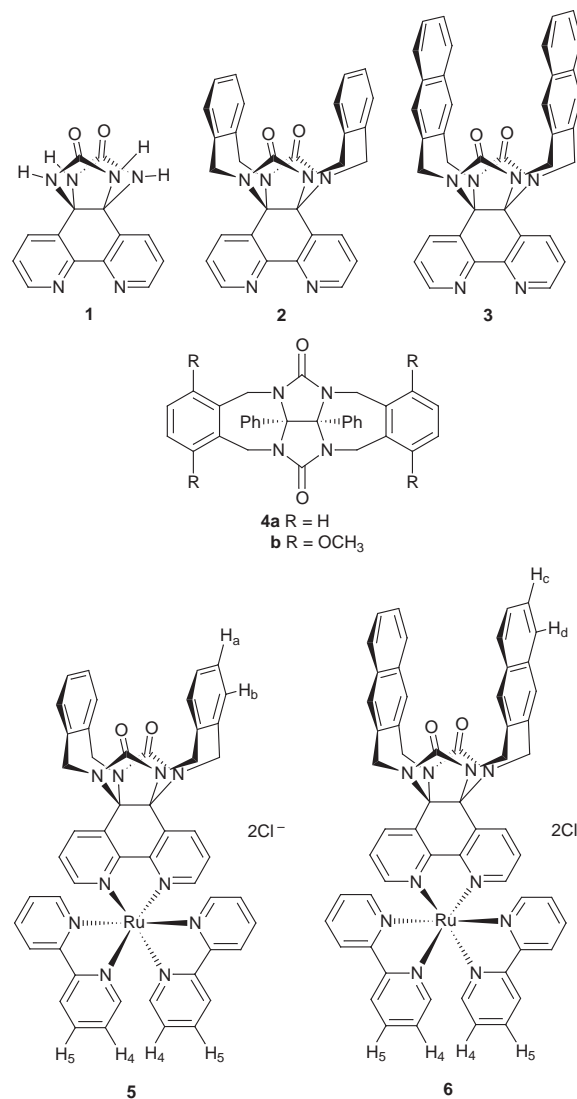
Bipyridine-glycoluril **1** was prepared in 81% yield by acid catalyzed condensation of 1,10-phenanthroline-5,6-quinone⁴ and urea in toluene. Clip molecules **2** and **3** were synthesized in 32% and 16% yields, respectively, from **1** and 1,2-bis-(bromomethyl)benzene and from **1** and 2,3-bis(bromomethyl)naphthalene according to a standard procedure.^{3‡}

Single crystals of **2** were grown by slow diffusion of methanol into a chloroform solution of this compound.[§] The crystal structure [Fig. 1(a)] reveals that a large steric interaction exists between the γ -bipyridine and methylene protons of **2** resulting in a more squeezed cavity compared to cavities of other DPG-derived clips. This is reflected in the smaller distance between the aromatic side-walls of **2** (6.18 Å, as compared to 6.67 Å in the crystal structure of **4b**⁵). To investigate the consequences of this narrower cavity on the binding properties of **2** and **3** in CDCl₃, ¹H NMR binding studies with various 5-substituted 1,3-dihydroxybenzenes were carried out. It can clearly be seen in Table 1 that binding of guests in **2** is significantly weaker than in the reference compound **4a**, which is in agreement with the observed squeezed cavity of **2**. The host-guest binding properties of **3** in CDCl₃ are even weaker than those of **2**, as was observed before in DPG-derived clips containing 2,3-connected naphthalene walls.⁶

Clips **2** and **3** were then complexed with [Ru(bipy)₂]Cl₂·2H₂O⁷ to give water-soluble metalloclips **5** and **6** in 56% and 42% yields, respectively.[‡] ¹H NMR experiments indicated that when a solution of **5** in D₂O was diluted, the resonances of the wall protons H_a and H_b and the bipyridine protons H₄ and H₅ shifted downfield, whereas the resonances of all the other protons of **5** did not undergo significant shifts. From an NMR dilution titration (500 MHz) in D₂O, the self-association constant of two molecules of **5** was determined to be $K_{\text{dimer}} = 50 \pm 10 \text{ dm}^3 \text{ mol}^{-1}$; the same value was calculated for each shifting proton. A 2D NOESY experiment of **5** in D₂O

revealed several NOE contacts between the sidewall protons of one molecule of **5** and the bipyridine protons of its neighbour. Combining these results, we propose that **5** forms head-to-tail associates in water, clipping the sterically least hindered side of one of the bipyridine ligands of its neighbour between its cavity walls. From the calculated complexation induced shift values for the shifting protons (H_a: -0.85 ppm; H_b: -0.45 ppm; H₄: -1.41 ppm; H₅: -0.58 ppm), the geometry of the self-associated complex can be predicted, see Fig. 1(b). Because of steric hindrance it is not possible for **5** to bind simultaneously two neighbours at both bipyridines.[¶]

A ¹H NMR dilution titration of complex **6** in D₂O (0.1–2 mM) showed downfield shifts of the resonances of H₄, H₅, H_c and H_d. At concentrations above 2 mM the solutions of **6** became turbid and severe line broadening occurred, which was attributed to the



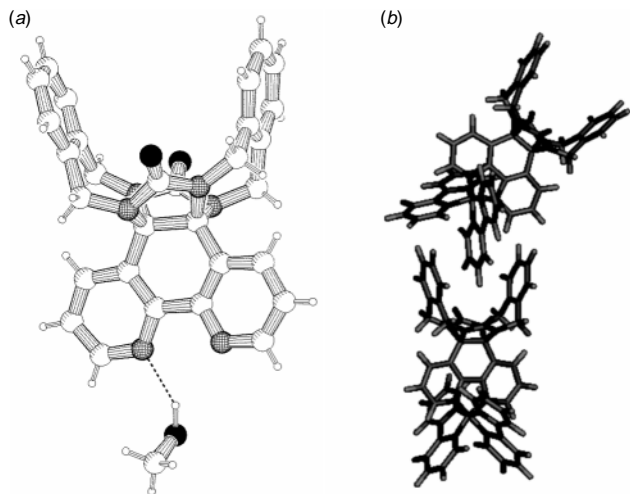


Fig. 1 (a) X-Ray structure of **2**-CH₃OH; (b) ¹H NMR based and computer generated (Quanta Charmm) structure of two molecules of **5** in D₂O

Table 1 Association constants (dm³ mol⁻¹) of complexes between various host and guest molecules in CDCl₃ (*T* = 298 K)

Guest	Host		
	2 ^a	4a ^b	3 ^a
5-Pentylresorcinol	20	74	<5
Resorcinol	50	175	— ^c
5-Methoxyresorcinol	60	195	— ^c
5-Chlororesorcinol	100	475	— ^c
Methyl 3,5-dihydroxybenzoate	100	850	20
5-Cyanoresorcinol	240	3500	— ^c

^a Estimated errors 20%. ^b Values taken from ref. 6. ^c Not determined.

formation of larger aggregates (*vide infra*). The calculated K_{dimer} using H_c or H_d as a probe (21000 ± 5000 dm³ mol⁻¹) was much larger than the calculated K_{dimer} using H₄ or H₅ as a probe (2500 ± 500 dm³ mol⁻¹). These values indicate that **6**, in contrast to **5**, can self-associate in two competing geometries, *viz.* head-to-head and head-to-tail, in which the interaction between the large hydrophobic cavities of **6** in the former geometry is stronger than the clipping of a bipyridine ligand between the cavity side-walls in the latter. The existence of both head-to-head and head-to-tail geometries has been observed before in the case of naphthalene-walled pyridinium-functionalized clips.³ The self-association of **6** in D₂O is much stronger than the self-association of **5**, which is in contrast with the binding of guests in CDCl₃ solution, where **2** is a better host than **3**. In aqueous solution, however, the self-association geometry is dominated by hydrophobic interactions, and since **6** has a much larger hydrophobic cavity than **5** it is expected that **6** forms stronger self-associated complexes.

To further study the aggregates formed, samples of **5** and **6** in D₂O were investigated by electron microscopy (TEM). For **5**, rather undefined scroll-like structures were observed with lengths up to 10 μm [Fig. 2(a)]. In contrast, for **6**, well defined 'cigar-like' aggregates were found [Fig. 2(b),(c)] which displayed a very high monodispersity in size [aspect ratio (length/width) = 11 ± 2]. X-Ray powder diffraction on samples of **5** and **6** revealed no clear reflections, implying that the aggregates are built up from molecular units that interact in a very diverse way or assemble in a variety of geometries. Since the complexes are racemic mixtures of Λ and Δ enantiomers, and in the head-to-tail self-association geometry one molecule of **5** or **6** has the possibility to choose between different bipyridine ligands of a neighbouring clip molecule for binding in its cleft and, additionally, has the option to use each of its own bipyridines to hold another clip molecule, such diversity in binding can be easily envisaged.

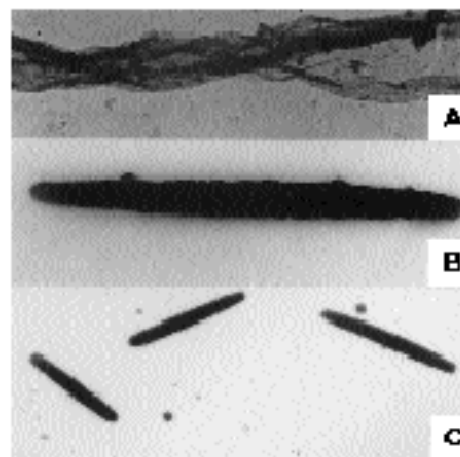


Fig. 2 Electron microscopic pictures of aggregates formed by **5** and **6** in water: (a) TEM picture of a scroll formed by **5**, 1 cm = 100 nm; (b),(c) TEM pictures of 'cigar-like' aggregates formed by **6**, 1 cm = 500 nm (b), 1 cm = 1750 nm (c). No shadowing or staining techniques were applied.

The observation that **6** assembles into a better defined supramolecular structure than **5** is attributed to the stronger self-association behaviour of **6**. We propose that the molecules of **6** self-assemble in a similar fashion to that reported before for the 'razorblade-like' nanostructures formed by molecular clips with pyridinium functions.³ With their large hydrophobic cavities, molecules of **6** initially form head-to-head dimers, to which monomers of **6** can be further attached in a head-to-tail fashion. In this way, assemblies are formed that always have a hydrophilic outer surface. What is unique about these assemblies is that they grow until they reach a finite size. Apparently, at a certain point further growth is no longer energetically favoured.

Preliminary fluorescence experiments on solutions of both **5** and **6** in water indicate that upon excitation of the CT band the emission is quenched at higher concentrations due to aggregate formation. Further studies aimed at understanding the mechanism of assembly and the photophysical and electrochemical properties of the 'cigar-like' aggregates are in progress and will be reported in a forthcoming full paper.

Notes and References

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‡ All new compounds were fully characterized. Full experimental details will be reported in a forthcoming full paper.

§ *Crystal data* for **2**-CH₃OH: C₃₁H₂₆N₆O₃, M_r = 530.58, space group $P2_1/n$, monoclinic, a = 10.5690(3), b = 18.2221(5), c = 12.9211(2) Å, β = 92.241(2)°; V = 2486.57(10) Å³, Z = 4, ρ_{calc} = 1.364 g cm⁻³; $2\theta_{\text{max}}$ = 139.92°, Cu-K α radiation (graphite monochromator) λ = 1.54184 Å, μ = 0.765 mm⁻¹, T = 293(2) K, scan type: θ - 2θ ; 4974 reflections collected, 4710 independent of which 4016 observed. Final $wR2$ = 0.1078, final $R1$ = 0.0410 [for $I > 2\sigma(I)$]. CCDC 182/906.

¶ A 1:1 self-association is also supported by the data of the dilution titration, which could only be fitted by assuming a 1:1 complex.

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