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Thermodynamically driven self-assembly of pyridinearene to hexameric capsules†

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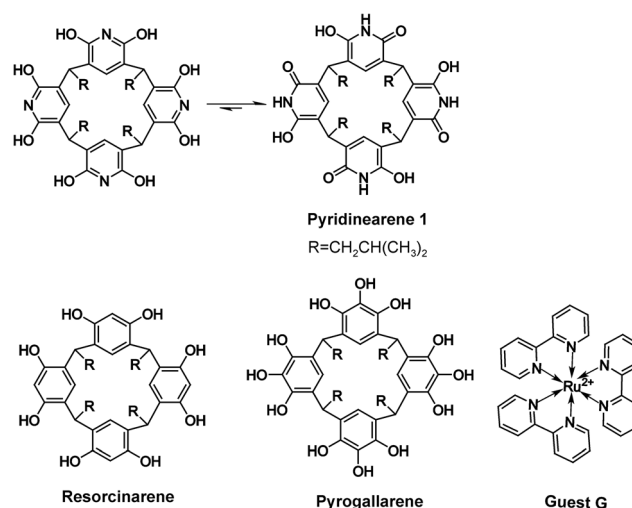
Pyridinearene macrocycles have previously shown unique host-guest properties in their capsular dimers including *endo* complexation of neutral molecules and *exo* complexation of anions. Here, we demonstrate for the first time the formation of hydrogen bonded hexamer of tetraisobutyl-octahydroxypyridinearene in all three states of matter – gas phase, solution and solid-state. Cationic tris(bipyridine)ruthenium(II) template was found to stabilize the hexamer in gas phase, whereas solvent molecules do this in condensed phases. In solution, the capsular hexamer was found to be the thermodynamically favoured self-assembly product and transition from dimer to hexamer occurred in course of time. The crystal structure of hexamer revealed 24 N–H...O direct intermolecular hydrogen bonds between the six pyridinearene macrocycles without any bridging solvent molecules. Hydrogen bond patterns correlate well with DFT computed structures. Thus, all structural chemistry methods (IM-MS, DOSY NMR, DFT, X-ray crystallography) support the same structure of the hexameric capsule that has a diameter of ca. 3 nm and volume of 1160 Å³.

long known for their capability to spontaneously self-assemble into large hexameric capsules.² Interestingly, the hydrogen bonding network in resorcinarene hexamers typically involve bridging solvent molecules, which might even be responsible for their unique catalytic activity.⁴ Both resorcinarenes and pyrogallarenes have demonstrated their ability to encapsulate various guest molecules in the voids of their capsular dimeric and hexameric assemblies.^{2,3}

Pyridinearene⁵ (**1** in Scheme 1) is closely related to resorcinarene and pyrogallarene. Despite their obvious structural similarities, pyridinearenes display different binding properties due to amide-iminol tautomerism and electronic properties arising from the pyridine ring.⁶ From the two tautomeric forms, dihydroxy and hydroxy-oxo, only the latter has been observed in crystal structures.⁶ Recently, conformational analysis for the tautomers also revealed that the hydroxy-oxo

Introduction

Capsular supramolecular structures are tempting species, as they enable encapsulation of guest molecules and their voids may act as confined spaces suitable for nanocatalysis.¹ Resorcinarenes and pyrogallarenes (see Scheme 1), have been



Scheme 1 Structures of tetraisobutyl-pyridinearene **1**, tris(bipyridine) ruthenium(II) guest (**G**), resorcinarene and pyrogallarene. For pyridinearene two tautomeric forms are shown, but equilibrium is greatly favoring hydroxy-oxo tautomer.

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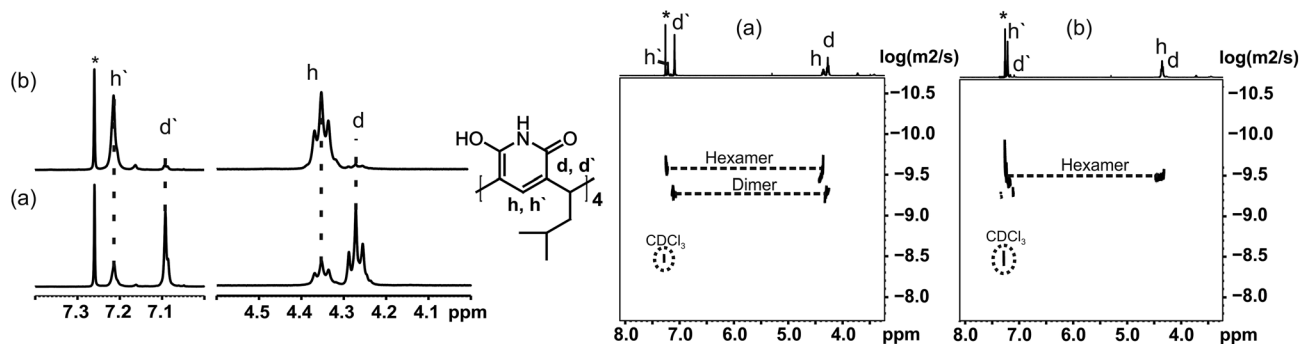


Fig. 2 Left: ^1H NMR of **1** (20 mM in CDCl_3) (a) measured within 2 hours after sample preparation and (b) same sample after 7 days from sample preparation. Right: DOSY NMR of the same sample (a) measured within 2 hours from sample preparation and (b) after 7 days from sample preparation. Signals d and d' correspond to the dimeric assembly and signals h and h' to the hexameric assembly.

values are also well in line with the observed gas phase structures and determined CCS values. The DOSY NMR experiment in Fig. 2a was measured within 2 hours after sample preparation and shows the dimeric assembly as more abundant (2 : 1). The same NMR sample was stored and re-measured after seven days showing that the intensity of the signals for the dimer diminished dramatically, while at the same time signals for the hexamer increased and were now dominating (ratio $d : h$ 1 : 10). This can also be seen in DOSY NMR, where only the signal of hexamer is observed after 7 days from sample preparation (Fig. 2b). This shows that pyridinearene forms indeed both dimeric and hexameric capsules in solution but the dimeric capsule is obviously only the kinetically favoured product while the hexameric capsule is the thermodynamic product, which abundance increases over time.

Single crystals suitable for X-ray diffraction analysis were obtained by slow vapour diffusion of diisopropyl ether into the solution of **1** in chloroform. Block shaped crystals were formed and the hexamer structure (**1**₆) in the solid-state could be confirmed by X-ray crystallography (Fig. 3a). The asymmetric unit contains three crystallographically independent molecules of **1**, and the resultant self-assembled hexameric structure contains 24 O–H...O and 24 N–H...O hydrogen bonds. As a result of hydroxy-oxo tautomer form, the 6-hydroxyl position in 6-hydroxy-2(1*H*)-pyridone units manifest four O–H...O circular intramolecular hydrogen bonds to give **1** bowl-like C_{4v} conformation. The intermolecular N–H...O hydrogen bonding between the pyridone units in **1**₆ provides a compact internal cavity with volume of 1160 Å³. This is smaller than corresponding hexameric capsules based on resorcinarenes and

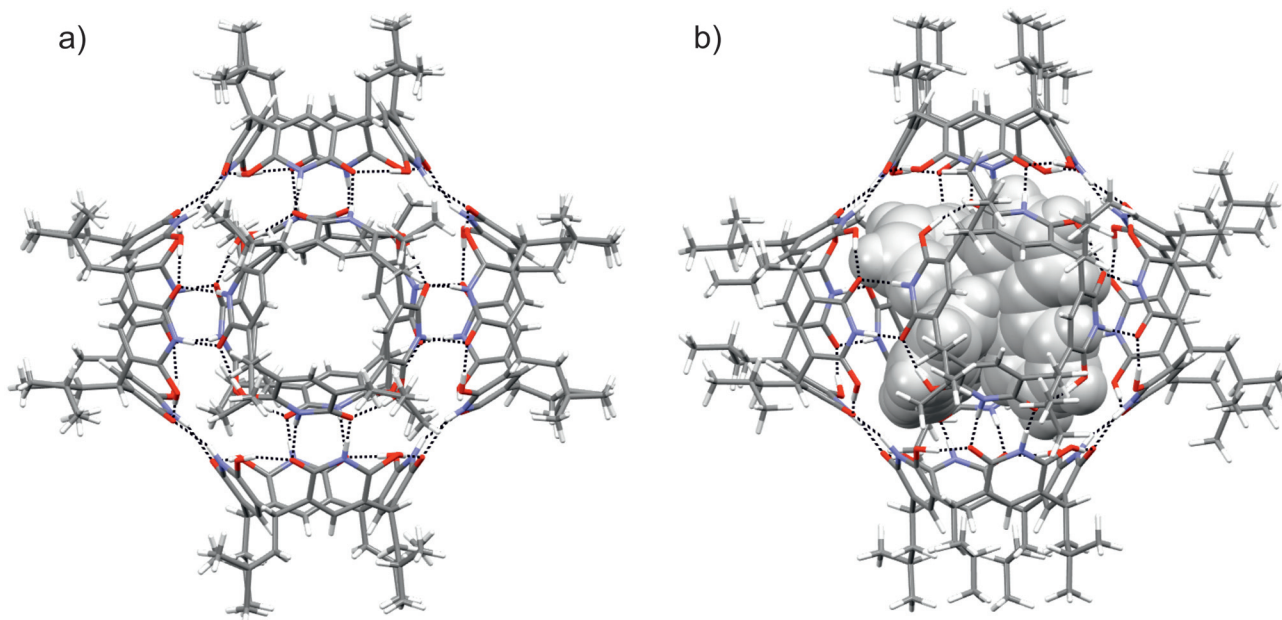


Fig. 3 X-Ray crystal structure of **1**₆ and (b) optimized structure of **[1**₆ + **G**]²⁺ at the RI-PBE-D3/def2-SVP level of theory in capped stick model. Tris (bipyridine)-ruthenium(II) (**G**) is shown in grey CPK model in (b). Black dashed lines represent hydrogen bonds. Color code: H = white, C = grey, N = blue, O = red.



Conflicts of interest

There are no conflicts to declare.

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Notes and references

‡ Please note, that the template G is not necessary to observe the hexameric assembly in (+)ESI-MS. Without templating guest hexamer can be observed as $[1_6 + Na]^+$ even in low (20 μ M) concentration, but with relatively lower abundance (see Fig. S1†).

§ $^{DT}CCS_{He}$ states for CCS values obtained using drift tube instrument with helium gas, nomenclature recommended in V. Gabelica *et al.*²⁵

¶ $^{DTM}CCS_{He}$ states for CCS values obtained using diffuse trajectory method with helium gas.

|| According to Mason-Schamp equation, different gases result in different drift times, and thus to different CCS values. For more detailed explanation see V. Gabelica and E. Marklund.²⁶

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