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A molecular chalice with hydrophobic walls and a hydrophilic rim: self-assembly and complexation properties†‡

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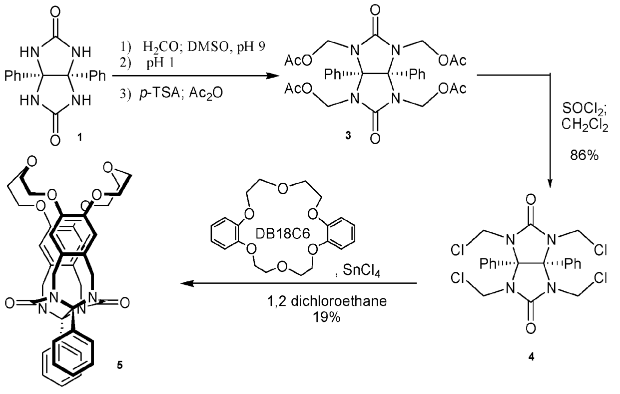
We describe the synthesis of a diphenylglycoluril/dibenzo-crown-6 molecular chalice, the self-assembly at the air/water interface and its complexation properties in solution and at the water/chloroform interface.

Molecular recognition at interfaces has relevance to biological systems but is also important for modern applications such as high sensitivity sensors. Selective binding of guest molecules in solution to host molecules located at a solid surface has been described during the past two decades using Langmuir monolayers, self-assembled monolayers and lipid assemblies as recognition media.[1] Diphenylglycoluril[2] **1** is a rigid, concave molecule which can be easily functionalized in order to obtain excellent building blocks for synthetic molecular clips and tweezers with interesting molecular recognition properties, such as self-assembling and molecular recognition of small electron-deficient guest molecules.[3] On the other hand, crown ethers as macrocyclic polydentate ligands are used most often as a catalyst in phase transfer processes[4] by forming complexes with inorganic salts. Their polyfunctionality makes them particularly useful for the construction of various supramolecular systems,[5] to optically control the extraction of ions, as elements of photo-switchable molecular devices, or as novel materials for recording, storing, and processing optical information.[6] The combination of diphenylglycoluril with crown ethers has been previously described for the synthesis of molecular baskets, where crown ethers were used as handles.[7]

Here we report the design, synthesis and properties of a chalice-shaped molecular receptor, with a diphenylglycoluril bottom and a crown ether rim. Because of the duality of the polar rim and the hydrophobic walls, as well as the particular rigidity, we were interested in the extraction properties and ability to form monomolecular films at the water/organic solvent interface of this molecule. The first synthetic steps outlined in Scheme 1 were previously reported in the literature for preparing **4** from diphenylglycoluril.[8] The final step in the synthesis of **5** is the addition of the aromatic side walls and the crown ether moiety by a quadruple Friedel–Crafts reaction of **4** and the dibenzo[18]crown-6 (DB18C6). As side products of this reaction, mono- and double-attached DB18C6 were formed, as previously reported for Friedel–Crafts reactions with **4**.[8] Due to its particular shape, one of the most promising applications of this molecular chalice would be cation recognition and application in separation processes. Crystals of molecular chalice **5** suitable for X-ray crystal structure determination were obtained by diffusion of ether to a chloroform solution of **5** (CCDC 831478).



Scheme 1 Synthesis of molecular chalice **5**.

The aromatic walls define a squared cavity, with the centers of the benzene rings at 5.32 Å distance (Fig. 1). The two fused five-member rings of glycoluril form an electron rich shallow floor, with two hydrogen bond acceptor sites (two carbonyl oxygen atoms) separated by 5.56 Å. The most unusual structural feature of **5** lies in the asymmetric conformation of the crown ether moiety, which may bind only small alkali metals, compared to the free DB18C6.

Alkali metal complexation in solution was followed by NMR. If for Na^+ and K^+ cations complexation can be observed by NMR, no significant NMR chemical shifts were observed for Rb^+ or Cs^+. While an upfield shift is generally

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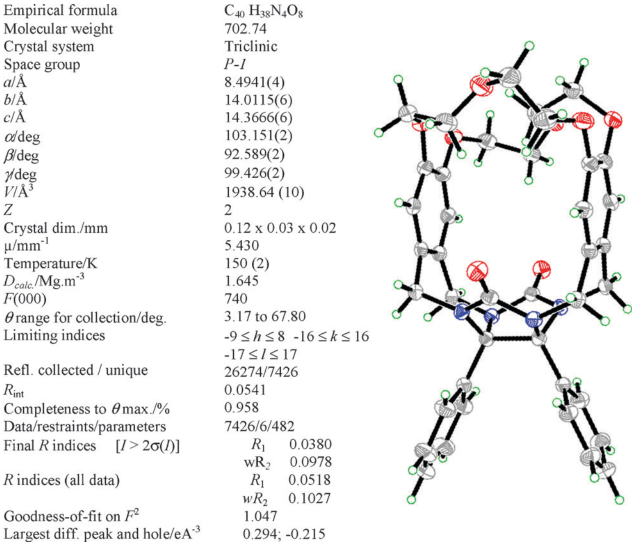

Empirical formula	$C_{40}H_{38}N_4O_8$
Molecular weight	702.74
Crystal system	Triclinic
Space group	*P-1*
a/Å	8.4941(4)
b/Å	14.0115(6)
c/Å	14.3666(6)
α/deg	103.151(2)
β/deg	92.589(2)
γ/deg	99.426(2)
V/Å^3	1938.64 (10)
Z	2
Crystal dim./mm	0.12 x 0.03 x 0.02
μ/mm^{-1}	5.430
Temperature/K	150 (2)
$D_{calc.}$/Mg.m^{-3}	1.645
F(000)	740
θ range for collection/deg.	3.17 to 67.80
Limiting indices	$-9 \leq h \leq 8$ $-16 \leq k \leq 16$ $-17 \leq l \leq 17$
Refl. collected / unique	26274/7426
R_{int}	0.0541
Completeness to θmax./%	0.958
Data/restraints/parameters	7426/6/482
Final R indices $[I > 2\sigma(I)]$	R_1 0.0380 wR_2 0.0978
R indices (all data)	R_1 0.0518 wR_2 0.1027
Goodness-of-fit on F^2	1.047
Largest diff. peak and hole/eA^{-3}	0.294; -0.215

Fig. 1 ORTEP view of **5** (ellipsoids are drawn at 30% probability level).

obtained when a metal is complexed by a crown ether, due to the electron withdrawing effect of the metal, during the titration of **5** with $NaPF_6$ or KPF_6, an upfield shift of the multiplet at 3.64–3.55 ppm and a downfield shift of the multiplet at 4.36–4.28 ppm can be observed. This suggests that the cation complexation induces a conformation change of the crown ether moiety, and the chemical shifts are a combination of the electron withdrawing effect and geometry change. Indeed, as shown in the crystal structure of **5**, the crown ether's conformation is not symmetrical, with one oxygen atom pointing towards the exterior of the cavity and the other oxygen atom pointing towards the interior of the cavity. The complexation may induce a conformation where both oxygen atoms point outside the cavity to chelate the cation. From the variation of the chemical shifts of H_1 and H_2 protons in the ^{1}H NMR spectra, Job's plots were drawn and the maximum observed at 50% of the total concentration and the shape of the curve revealed a 1 : 1 stoichiometry (see ESI†). To determine the association constants, NMR titrations were done with solutions having a constant concentration of **5** and varying concentrations of $NaPF_6$ or KPF_6. By the non-linear curve-fitting methods,[9] the association constant for a **5**:**Na**$^+$ complex was estimated to be about 1350 ± 80 M^{-1} and 500 ± 28 M^{-1} for **5**:**K**$^+$. If for Na^+ the association constant is 20 times lower than the one for DB18C6 with Na^+, for K^+ the association constant of **5** is 200 times lower than that for the corresponding crown ether. The crown ether moiety of **5** clearly distinguishes between the Na^+ and K^+ cation, with a higher selectivity for Na^+.

The amount of picrate ions extracted by **5** from an aqueous solution was analyzed by the difference in UV spectrophotometric absorbance of the aqueous solutions before and after extraction with a chloroform solution containing the macrocycle.[10] DB18C6 ether was used as a control macrocycle, which extracts only sizeable amounts of the potassium picrate, in agreement with previous reports.[11] Inspection of the data presented in Table 1 reveals that **5** displays low selectivity toward extraction of K^+, Rb^+ and Cs^+ picrates from aqueous solution, but a high selectivity for Na^+, compared to DB18C6.

Table 1 Alkali metal picrates extraction data

	Percentage of picrate extracted			
Host[a]	Na^+	K^+	Rb^+	Cs^+
DB18C6	0.25 mM 5.1%	2.03 mM 40.6%	1.20 mM 23.9%	0.49 mM 9.8%
5	0.75 mM 15%	0.07 mM 1.5%	0.04 mM 0.8%	0 mM 0%

[a] Extraction conditions: 5 mM of **5** or DB18C6 in water-saturated $CHCl_3$ solvent. The aqueous phase was 5 mM in alkali metal picrate. Values given are the average of 3 independent extraction experiments. Extraction samples were shaken for 0.5 h at r.t. and allowed to equilibrate for 12 h prior to undertaking UV spectrophotometric analysis of the aqueous phase at 374 nm.

It is not surprising that the alkali metal selectivity is completely different when comparing the conformation of free DB18C6 and the crown ether moiety of **5**.[12] But the most interesting observation of this extraction process is that the molecular chalice **5** is absolutely not soluble in water, and the extraction takes place at the interface. Only in the presence of sodium or potassium picrates, precipitates were formed at the water–chloroform interface, showing that the molecular recognition took place at this interface (see ESI† Fig. S3: different surface tension properties can be observed for the different alkali metal picrate solutions). The discrimination ability of **5** towards Na^+ compared to K^+ is also reflected by the amount of precipitate formed at the interface during the extraction process.

In order to understand the 2D organisation of **5** at an interface, a solution of the molecular chalice was spread on a pure water surface from a 1 mM solution in chloroform. The film structure was investigated by means of π–A isotherms and microscopic observation of the textures of Langmuir monolayers was possible by Brewster Angle Microscopy (BAM) and ellipsometric microscopy techniques.[13] The surface pressure/area compression isotherms of **5** are shown in Fig. 2, where it can be seen that chalice molecules form a coherent monolayer film. The complete isotherm shown in Fig. 2 was obtained by combining and correcting the different isotherms obtained when spreading different volumes of the same 1 mM solution of **5**. Since chalice **5** is not a classical amphiphile, this strategy was necessary to fully understand its behaviour at the air–water interface. The film remains in a gaseous phase (0 mN m^{-1})

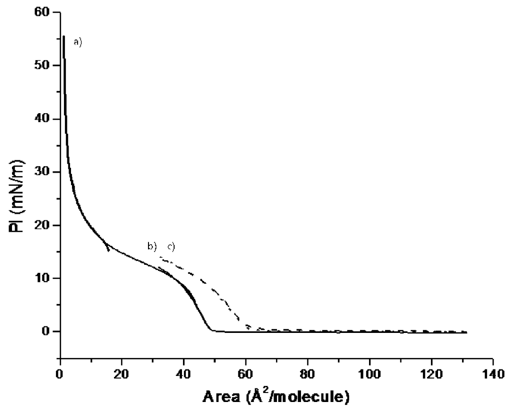

Fig. 2 Surface pressure (π)/molecular area isotherms of **5** on (a) pure water; (b) NaCl 10 mM solution and (c) KCl 10 mM solution.

until a molecular area of ~50 Å^2 per molecule is reached, when an increase in pressure was observed. The slope suggests that the film reached a condensed phase at that point. At ~40 Å^2 per molecule (corresponding to the cross-sectional area of **5** ~42 Å^2 in the crystal structure), the change of the slope represents the reorganization of the film structure, indicating controlled collapse of the monolayer towards multilayers formation. As molecular chalice **5** showed a high selectivity for sodium cations in solution, a solution of **5** was spread on a 10 mM NaCl subphase from a 1 mM solution in chloroform (Fig. 2). The isotherm shows a significant shift to higher molecular areas, however, when higher volumes of **5** were spread on the 10 mM NaCl subphase, *i.e.* isotherms starting at 40 Å^2/molecule, the isotherms are identical in both the presence and absence of NaCl. This suggests that the molecular chalice may complex sodium in the monolayer state *i.e.* before the first reorganization transition but upon spreading into a multilayer, either the sodium cation is not incorporated in the layers or does not affect their organization. Having said this, the same isotherms were obtained when spread on a 10 mM KCl subphase, which indicates that the behaviour of **5** at the air–water interface is not affected by the nature of the cation. Thus complexation may not induce a conformation change of the monolayer at the interface and counterions may additionally interact non-specifically with the chalice to expand the monolayer. BAM was utilized to characterize the morphology of films of **5** during the course of compression in the absence of ions (see ESI†, Fig. S4). High molecular areas showed large regions of material which was already aggregated. Once the pressure began to increase, the film appears to comprise a uniform distribution of aggregates of varying heights and/or optical properties. Only once the plateau is reached does it appear that the gaseous phase is completely removed and the aggregates have coalesced.

In order to confirm this organization, spectroscopic ellipsometry was used to determine the thickness of a Langmuir–Blodgett film deposited at 5 mN m^{-1} on silicon. Seven ellipsometric thicknesses at different locations of the LB film were measured, giving an average of 12.3 ± 0.2 Å. Thus, this result suggests that the molecular chalices form a monolayer, knowing that the distance from the crown ether moiety and the phenyl groups in the crystal structure is 12.86 Å (Fig. 1). AFM was used to investigate the structure of the Langmuir–Blodgett film when deposited on a mica surface. When transferred during the first regime compression at $\pi < 10$ mN m^{-1} at 25 °C, a film is formed with a height of 12.1 ± 0.4 Å (measured at seven different pinhole locations), corresponding to the formation of a monolayer (Fig. 3). When the films are transferred at $\pi > 20$ mN m^{-1} at 25 °C the underlying monolayer is more continuous and uniform (with the absence of pinholes and less height variation). Furthermore the observed aggregates are 26.1 ± 0.4 Å above the background monolayer, indicating the formation of a double layer.

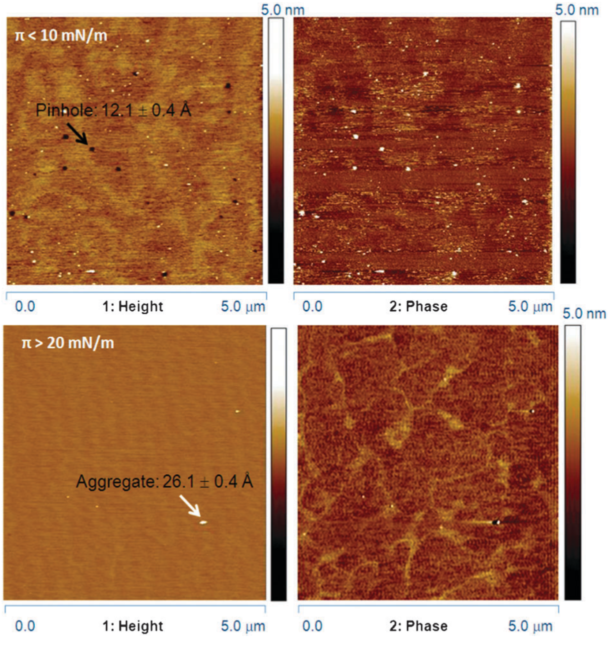

Fig. 3 AFM images of the film transferred onto mica.

In conclusion we have synthesized and characterized a molecular chalice able to selectively bind Na$^+$ cations. This unique molecular recognition property should be useful for future technology, for example in creating new chemical sensors and in fabricating two-dimensional molecular lattices comprising multiple functional units for molecular separations and water depollution.

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