Molecular Recognition

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Selective Binding and Easy Separation of C_{70} by Nanoscale Self-Assembled Capsules**

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Advances in the chemistry of higher fullerenes (> C_{70}) suffers from the limited availability of these molecular allotropes of carbon: even the combined amount of C_{60} and C_{70} produced by sooting flames is less than 9% of the soot mass.[1] Soxhlet-based solid–liquid extractions with toluene followed by evaporations and tedious chromatographic separations requiring large amounts of solvents are usually employed for the separation and purification of C_{60}/C_{70} mixtures.[2] A complete protocol for the separation of fullerenes by column chromatography and HPLC has been reported by Diederich and co-workers.[3] Most of the separation methods based on selective complexation with Lewis acids[4] or host–guest chemistry, such as encapsulation by cyclodextrins[5] or calix[8]arenes,[6] apart from their inherent elegance and esthetical appeal, are impractical because they are selective for the major component C_{60} but not for C_{70} or the higher fullerenes.[7] Although two examples of calixarenes showing selectivity for C_{70} over C_{60} have been reported, the release of the fullerene and simultaneous recovery of the valuable host from the complex proved difficult or required the use of chromatography.[8]

This problem could be circumvented by using hydrogen-bonded, self-assembled curved host structures that encapsulate or fully wrap around the guest,[9] but easily dissociate into smaller, noncomplexing fragments upon disruption of the capsule with polar solvents or under the influence of acids. We report herein the self-assembling module **1** that reversibly forms a dimeric capsule of nanoscale dimensions (ca. 17 × 14 Å, inner volume ca. 790 Å^3) by combining the curvature of cyclotriveratrylene (CTV) and three high-affinity hydrogen-bonding units. The resulting spherical host shows high selectivity for fullerenes and can be used to purify C_{70} efficiently from crude soot or fullerite mixtures by simple solid–liquid extractions. Furthermore, enriched mixtures of higher fullerenes, such as C_{76}, C_{78}, C_{82}, and C_{84}, are obtained.

In the early 1990s, Atwood and co-workers reported the formation of so-called "ball and socket" complexes between CTV and C_{60}.[10] These C_{60}@CTV complexes were shown to have a 1:1 complexation stoichiometry in solution and to form either 1:1 or 1:1.5 complexes in the crystalline state.[11] However, 2:1 complexes of CTV with C_{60} have been described only rarely.[12] For the current intermolecular self-assembly we selected the 2-ureido-4-[1*H*]-pyrimidinone scaffold (UPy),[13a,b] one of the strongest hydrogen-bonded self-complementary units, which contains quadruple hydrogen bonds in a favorable DDAA (D donor, A acceptor) sequence and results in a high dimerization constant in apolar media (K_{dim} ($CHCl_3$) $\geq 10^7\,\mathrm{M}^{-1}$).[13c] Consequently, UPy dimers have been employed frequently as noncovalent bonding subunits to construct supramolecular architectures, such as polymers[14] and oligomeric cyclic aggregates (rosettes),[15] among others.[16]

The synthesis of the CTV-UPy host **1** was straightforward (Scheme 1) and could be performed on a gram scale. 2-Amino-4-[1*H*]-pyrimidinone (**2**), prepared from the corresponding β-ketoester and guanidine,[15] was activated as the imidazolide **3** with 1,1′-carbonyldiimidazole in tetrahydrofuran (THF)[17] and then treated with the tris(ethylamino)-CTV **4** (synthesized from triol **5**[18] in three steps via a triazide intermediate) in dichloromethane at 50 °C to yield **1** in 92–94% yield (see the Supporting Information).

Host **1** is almost insoluble in toluene, but was easily dissolved by sonicating a solution containing C_{60} or C_{70}. The increased solubility was probably caused by the formation of relatively apolar hydrogen-bonded dimeric capsules of the host (**1**$_2$) around the fullerene. In the presence of 0.5 mol equivalents of C_{70}, the ^{1}H NMR spectra of **1** in different solvents (Figure 1) showed the presence of a complex mixture of aggregates, but in carbon disulfide a well-defined dimer was predominant. Downfield signals at $\delta = 13.12$, 10.89, and 10.16 ppm, a signature of the dimeric UPy urea protons,[13a,b] were evident.

Spectra recorded in deuterated tetrachloroethane ([D$_2$]TCE) at different temperatures revealed the dynamic nature of the host–guest system in this solvent. At 100 °C the capsule is presumably empty, although dimeric (**1**$_2$) or aggregated, as inferred from the absence of downfield-shifted sharp signals for the NH protons. In the case of C_{60} complexation, the equilibrium between empty and filled capsules was

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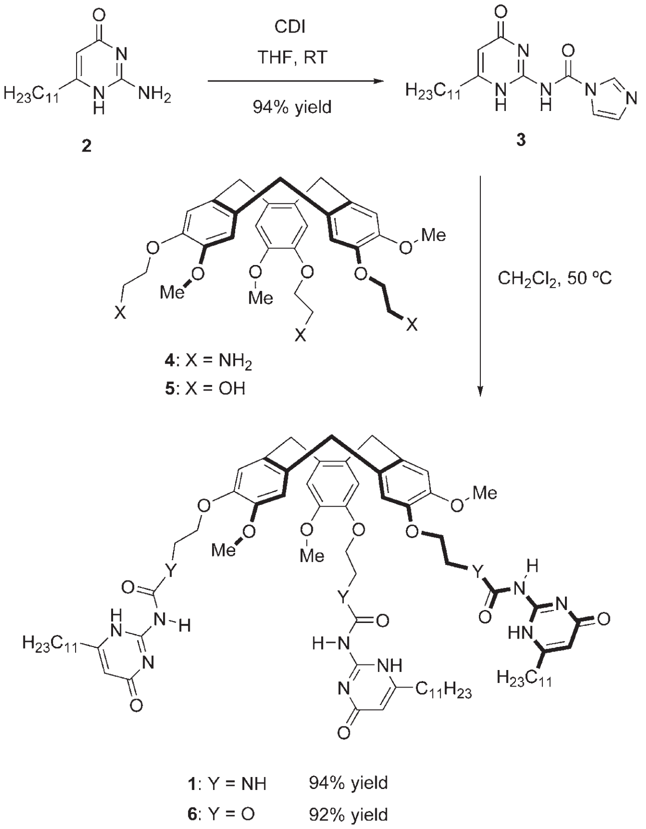
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.



Scheme 1. Synthesis of the CTV-UPy hosts. CDI = 1,1′-carbonyldiimidazole.

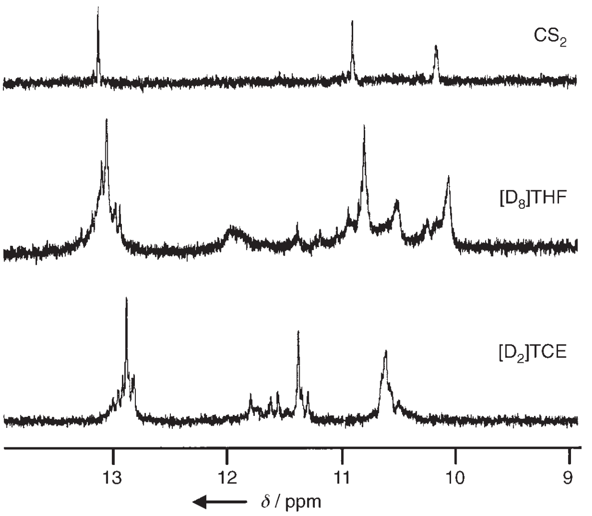


Figure 1. NH area ($\delta = 9$–14 ppm) of the ^{1}H NMR spectra (400 MHz) of **1** (5 mM) in different solvents in the presence of 0.5 equivalents of C_{70}.

evident with the naked eye, since solutions turned from red-brown (complex) to purple (free fullerene) on heating. The signals sharpened upon decreasing the temperature, but broadened again at −30 °C because of the restriction in the conformational mobility of the alkyl chains.

The stoichiometry of the complexes in TCE was determined by UV/Vis spectroscopy by measuring the concentration of the complex at different molar fractions of the host and guest (Job plots). Whereas the stoichiometry was found to be concentration-dependent for C_{60} (a maximum at a molar fraction of 0.33, typical of the formation of a 2:1 complex, was obtained at 1.5 mM, but mixtures of 1:1 and 2:1 complexes were found at lower concentrations), only 2:1 complexes were observed for C_{70} at all the concentrations studied, thus suggesting that the association constant K_a for C_{70} is significantly higher. Indeed, UV/Vis titrations in TCE at a constant fullerene concentration of 1.5 mM, followed by a nonlinear regression fitting of the data for a 2:1 binding model resulted in K_a (C_{60}) = $(1.93 \pm 0.13) \times 10^6\,\text{M}^{-2}$ and K_a (C_{70}) = $(7.4 \pm 4.5) \times 10^7\,\text{M}^{-2}$, which translate into 1.82×10^3 and $3.89 \times 10^4\,\text{M}^{-1}$, respectively, if the data are fitted for a 1:1 (capsule/guest) binding mode. In the 2:1 binding model, the observed constant is K_3 (M^{-2}) = $K_1 \times K_2$, where K_1 (M^{-1}) represents the binding of the guest with monomeric **1** whereas K_2 (M^{-1}) is the binding of this complex with another host **1** subunit. However, use of carbamate **6** (which can not dimerize) as a model to determine the contribution of K_1 revealed that no substantial binding with either C_{60} or C_{70} was observed, so the binding is likely due to a partial disruption of an initial $\mathbf{1}_2$ capsule or a dimeric aggregate to accommodate the guest, which is in good agreement with the values calculated for a 1:1 binding mode (see the Supporting Information).

The binding of fullerenes was also evaluated by isothermal titration calorimetry (ITC) in TCE. The binding constants and thermodynamic parameters (K (C_{60}) = $1.06 \times 10^4\,\text{M}^{-1}$ ($\Delta H = -4.1\,\text{kcal mol}^{-1}$; $\Delta S = 5.0\,\text{cal mol K}^{-1}$); K (C_{70}) = $4.45 \times 10^4\,\text{M}^{-1}$ ($\Delta H = -6.0\,\text{kcal mol}^{-1}$; $\Delta S = 1.5\,\text{cal mol K}^{-1}$)) are fully consistent with the values obtained by UV/Vis measurements, and are consistent with an enthalpically driven binding mode in both cases.

We used computational methods to rationalize the significantly higher binding constant for C_{70} over C_{60}. The geometries (Figure 2) were determined by means of a density

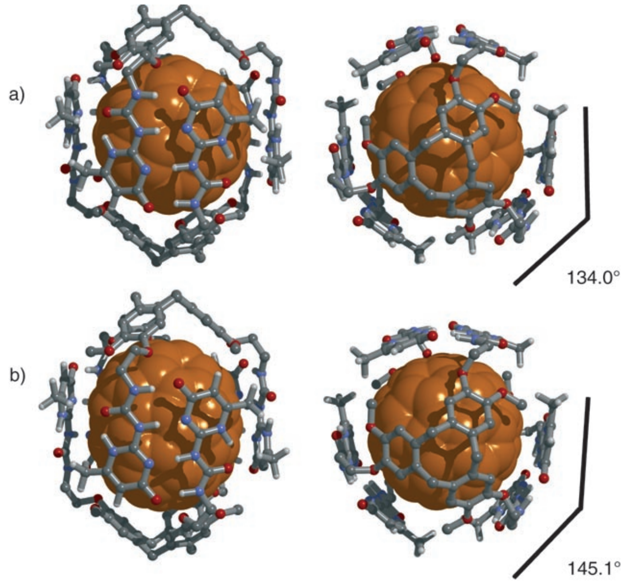


Figure 2. Side and top views of the DFT-calculated molecular structures of the: a) $C_{60}@\mathbf{1}_2$ and b) $C_{70}@\mathbf{1}_2$ hydrogen-bonded capsules.

functional method (DFT),[19] accurate enough to reproduce fairly well the geometry of the UPy dimer in the solid state,[20] and chosen as a compromise between accuracy and computational effort.

Hydrogen bonds maintain the two subunits at distances very similar to those observed in the model UPy dimer. Although the two subunits lie in the same plane in the case of the model, they are forced to adopt a bent shape in both cages. However, the angle formed by the two planes is closer to planarity in $C_{70}@\mathbf{1}_2$ (145.1°) than in $C_{60}@\mathbf{1}_2$ (134.0°) as a result of the narrower shape of the guest. Therefore, the hydrogen bonds are stronger for the C_{70}- than for the C_{60}-containing capsule, and more similar to the strength computed for an isolated UPy dimer. This difference might be the origin of the observed selectivity, as the host–guest interactions are very similar in both cases.

Based on the significant differences in the binding of C_{70} and C_{60} inside **1**, an experimental setup was designed to use **1** in the separation of mixtures of C_{60} and C_{70}, or eventually for the selective extraction of C_{70} directly from fullerene soot or from fullerite (the C_{60} and C_{70} enriched mixture arising from extraction of soot with toluene). THF was selected as the polar, aprotic solvent of choice since $\mathbf{1}_2$ is soluble in it, while common fullerenes have been reported to be insoluble.[21] We determined (HPLC measurements) the solubility of C_{60} in THF to be 18.0 $\mu g\,mL^{-1}$, but substantially much lower than in other ethers, such as diglyme, dioxane, tetrahydropyran, and dihexyl or dioctyl ether. Thus, extraction in THF ensures optimal selectivity, since the solubilization of the fullerenes should be mostly caused by encapsulation. Single solid–liquid extractions were performed by stirring a suspension of the fullerenes in a solution of **1** in dry THF (1 mL) for 15 minutes at room temperature, followed by filtration of the solids and analysis of the clean filtrate by reverse phase HPLC. Most of the fullerenes were extracted from the mixtures. For example, 43 % of the fullerenes was recovered from a 1:1:1 mixture of $C_{60}/C_{70}/\mathbf{1}_2$ in a C_{70}/C_{60} ratio of 87:13 (Table 1, entry 1), which means that 67 % of the C_{70} was extracted. The efficiency of the C_{70} recovery was clearly higher when the amount of C_{70} in the initial mixture was lower. Indeed, the use of fullerite (with a C_{60}/C_{70} ratio of 79:21) yielded mixtures with a 85 % recovery of the C_{70} from a single extraction. Even crude soot (containing ca. 7 % fullerenes) gave a C_{70}/C_{60} ratio of 54:46 after one extraction. On the other hand, selectivities were found to be dependent on both the fullerene ratios and amount of extractant employed (higher C_{70}/C_{60} ratios were obtained with lower percentages of C_{70} or extracting capsule).

Table 1: Fullerene extraction selectivities.[a]

Entry	Initial ratio of $C_{60}/C_{70}/\mathbf{1}_2$ [mol equiv]	Extract composition [% C_{70}][b]	Extract composition [% C_{60}][b]
1	1:1:1	87.26	12.74
2	1:1:0.5	96.38	3.62
3	1:12:11	99.31	0.69
4	6:1:1	92.47	7.53

[a] Measured by HPLC (Waters Symmetry C18 column, toluene/acetonitrile/methanol 60:20:20 by volume + 0.01 % TFA). [b] The inherent solubility of fullerenes in dry THF has been subtracted.

Release of the fullerenes from the capsule was exceedingly simple. Addition of a few drops of trifluoroacetic acid (TFA) to the THF solutions of the complexes caused the hydrogen-bonded network to break and the fullerenes to precipitate. The host could then be recycled by evaporation. Indeed, two consecutive extractions yielded an initial C_{70}/C_{60} mixture of 84:16 (from 20.9 mg of fullerite and 3.8 mg of host **1** in 2.0 mL THF), which turned into a 97:3 mixture upon addition of TFA, centrifugation, and re-extraction with 1.6 mg of **1**.

Most remarkably, higher fullerenes (from C_{76} to C_{84}) were also extracted in increased amounts over their initial content in the fullerite (< 2 %; Figure 3), likely because of the flexibility and adjustability of the capsule around the larger guests. This approach thus opens the way to an easy and practical access to these otherwise elusive materials.

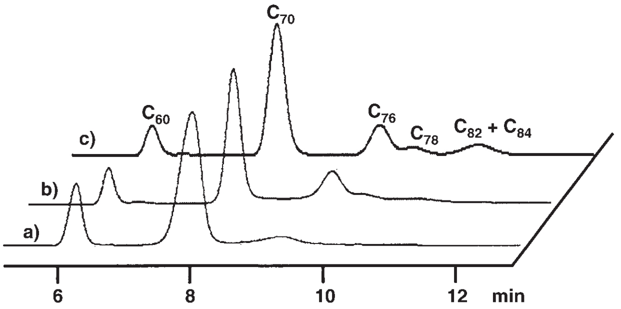


Figure 3. Fullerene ratios (from HPLC chromatograms) upon extraction of fullerite with various amounts of **1**. Percentage by weight of **1** relative to fullerite: a) 67 %, b) 34 %, and c) 18 %.

In conclusion, the combination of a concave cyclotriveratrylene host molecule **1** capable of complexing fullerenes with the strongly quadruple hydrogen-bonding ureidopyrimidinone unit resulted in a new host molecule that forms a well-defined dimeric hydrogen-bonded assembly that encapsulates a fullerene molecule within its large cavity. Noncovalently linked capsules based on CTV have not been reported so far. In addition, the system displays a remarkable selectivity for the encapsulation of C_{70} over C_{60}. By simple solid–liquid extractions, C_{70} with a purity of 97 % could be obtained from fullerite after only two runs. The unprecedented selectivity of **1** for the encapsulation of C_{70}, its simple isolation, and the easy access to enriched mixtures of higher fullerenes (C_{76}–C_{84}) paves the way for the discovery of novel applications of these elusive materials and the investigation of their chemical properties.

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