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Charge transfer and encapsulation in a synthetic, self-assembled receptor†‡

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Tetrathiafulvalene derivatives show charge transfer and exceptional binding within a self-assembled molecular capsule.

Reversibly-formed capsules are self-assembled receptors that temporarily sequester target molecules in the liquid phase. As the host more or less surrounds and isolates the guest, encapsulation provides a means to study individual molecules in small spaces, separated from the bulk solution but at equilibrium under ambient conditions.[1] Guest binding is driven by appropriate filling of the capsule's space and weak intermolecular forces, such as hydrogen bonding, aromatic stacking and solvophobic effects. Charge transfer interactions between host and guest are rarely encountered as a driving force for encapsulation;[2] we describe some cases here and report their effects on the association and photophysical properties of the assembly.

Cylindrical capsule $\mathbf{1_2}$ is a dimeric structure, held together by 8 bifurcated hydrogen bonds, offering an internal cavity of $\sim$460 Å^3 (Fig. 1).[3,4] Guest binding studies are normally performed in mesitylene (1,3,5-trimethylbenzene) as it is too large to fit comfortably in the space of $\mathbf{1_2}$.[5] Few guests can compete with small halogenated solvents, but certain anions—halides, PF_6^-, BF_4^-, IO_4^-—are forced into the capsule in dichloromethane or chloroform.[6]

Tetrathiafulvalene (TTF) derivatives, properly named 2,2′-bis(1,3-dithiolylidenes), are π-electron donors that form charge transfer complexes with many electron acceptors.[7] Some TTF derivatives, such as commercially available **2** and **3**, have appropriate shapes and sizes for the cavity, and these examples were used as encapsulation candidates (Fig. 2). The well-accommodated guest, *trans*-dimethylstilbene (**4**),[4,8] was used as a standard.

Guest binding inside capsule $\mathbf{1_2}$ is conveniently monitored by ^{1}H NMR spectroscopy, since encapsulation shifts the guest's signals dramatically upfield. Guest protons near the edges of the capsule are influenced by the magnetic anisotropy of the 8 aromatic rings and show $\Delta\delta$ of up to -5 ppm, while those near the middle show $\Delta\delta$ of about -1 ppm.[4]

^{1}H NMR binding studies of $\mathbf{1_2}$ with **2** and **3**, and stilbene **4**, were performed in CD_2Cl_2 and are summarized in Fig. 3. Capsule $\mathbf{1_2}$ is formed upon dissolution of **1** (10 μmol) in CD_2Cl_2, as illustrated by the sharp peaks in the ^{1}H NMR spectrum (Fig. 3a). It is expected that 3 or 4 solvent molecules occupy the capsule,[9] but the addition of one equivalent (5 μmol) of stilbene **4** to this solution gives a new signal at -2.80 ppm that corresponds to the methyl groups of **4** (Fig. 3b). The competition with solvent ($\sim$10 M) is evident, since two sets of peaks are present, in slow exchange on the NMR timescale. These peaks correspond to the $\mathbf{1_2 \cdot 4}$ (predominant) and $\mathbf{1_2} \cdot n CD_2Cl_2$ complexes.

The addition of one equivalent of **2** (5 μmol) to $\mathbf{1_2}$ in CD_2Cl_2 results in the appearance of two upfield peaks at -1.85 and -3.23 ppm, corresponding to the shielded methylenes of the guest (Fig. 3c). Again, capsule resonances corresponding to the ratio of $\mathbf{1_2 \cdot 2}$ (predominant) and $\mathbf{1_2} \cdot n CD_2Cl_2$ complexes are observed. Likewise, the addition of **3** (5 μmol) to $\mathbf{1_2}$ results in an upfield signal at -1.64 ppm, corresponding to the guest (Fig. 3d). Here, only one set of capsule peaks indicate that the $\mathbf{1_2 \cdot 3}$ complex is more favorable than either the $\mathbf{1_2 \cdot 2}$ or $\mathbf{1_2 \cdot 4}$ complexes. The addition of 2% DMSO to the $\mathbf{1_2 \cdot 2}$ and $\mathbf{1_2 \cdot 4}$ complexes and 6% DMSO to the $\mathbf{1_2 \cdot 3}$ complex causes the assemblies to dissociate, and the upfield resonances of the guests to disappear.

Pairwise competition experiments were performed with guests **2**, **3** and **4**, using ^{1}H NMR spectroscopy (Fig. 4). The guest exchange is quite slow; the end points of titration graphs a and b were taken as 400 and 1500 min, respectively, and are

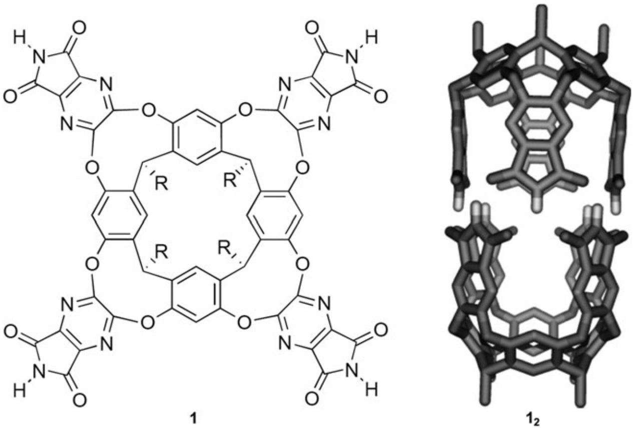

Fig. 1 Monomer **1** dimerizes in organic media to form cylindrical capsule $\mathbf{1_2}$. The C_{11} chains are removed in the model of the capsule.

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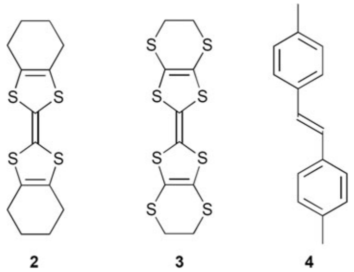

Fig. 2 TTF derivatives **2** and **3**, and known guest **4**.

not shown. For TTF **2** and the $\mathbf{1_2}\cdot\mathbf{4}$ complex (Fig. 4a), a twofold excess of $\mathbf{1_2}\cdot\mathbf{2}$, is present at equilibrium, clearly demonstrating that **2** is a better guest than **4**. With TTF **3** and $\mathbf{1_2}\cdot\mathbf{2}$ (Fig. 4b), all of the capsule is filled with **3** when equilibrium is reached. The reverse competition experiments produced identical results; even with 900 equivalents of **2** added to a $\mathbf{1_2}\cdot\mathbf{3}$ complex, only ~20% of $\mathbf{1_2}\cdot\mathbf{2}$ was observed at equilibrium. The complex formed with **3** is exceptionally stable.

Association constants were calculated by comparing the integral for the $\mathbf{1_2}\cdot$**guest** complexes to the $\mathbf{1_2}\cdot n\mathrm{CD_2Cl_2}$ complex. The $K_a(\mathrm{CD_2Cl_2})$ for $\mathbf{1_2}\cdot\mathbf{4}$ = 3.2×10^3 $\mathrm{M^{-1}}$ and the $K_a(\mathrm{CD_2Cl_2})$ for $\mathbf{1_2}\cdot\mathbf{2}$ = 1.3×10^4 $\mathrm{M^{-1}}$. The association constant for $\mathbf{1_2}\cdot\mathbf{3}$ was calculated using the competition data of **3** with $\mathbf{1_2}\cdot\mathbf{2}$, discussed above, and gave $K_a(\mathrm{CD_2Cl_2}) = 9.8 \times 10^7$ $\mathrm{M^{-1}}$. These K_a values agree with the competition experiments above. This strong association between **3** and capsule $\mathbf{1_2}$ in a competing solvent is unprecedented.‡

The ground state interaction of **2** and **3** with the capsule was evaluated using UV-vis spectroscopy (Fig. 5). The solvent-filled capsule absorbs <450 nm and has little to no color in solution, whereas **2** has a longer wavelength absorption (λ_{max} = 473 nm, ε = 300 $\mathrm{M^{-1}\,cm^{-1}}$) and appears yellow in solution. The addition of **2** to $\mathbf{1_2}$ gives a spectrum different from the sum of each component: a broad, long wavelength absorption (λ_{max} = 467 nm, ε = 1062 $\mathrm{M^{-1}\,cm^{-1}}$) appears over the course of 2 h. This is attributed to the formation of a charge transfer complex between the electron rich TTF guest and the electron poor capsule walls. The final equilibrated solution is orange/brown in color. Encapsulation of **3** results in a similar long wavelength absorption and color change. The addition of 2% DMSO to these complexes results in the disappearance of the charge transfer absorbance, and the solution color reverts to yellow as the capsule dissociates. The addition of 8 equivalents of the model wall **7** (Fig. 5, inset) to TTF **2** resulted in no change in the UV-vis spectrum, suggesting that encapsulation is essential for the formation of the charge transfer complex.

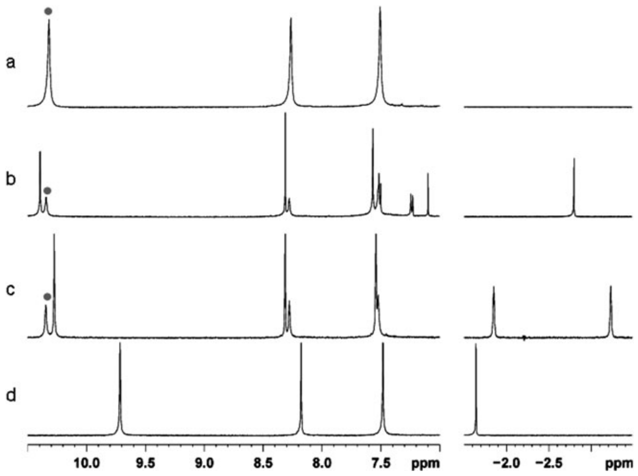

Fig. 3 ^{1}H NMR spectra of guests **2**, **3** and **4** encapsulated in $\mathbf{1_2}$ in $\mathrm{CD_2Cl_2}$ (1 mM): (a) $\mathbf{1_2}\cdot n\mathrm{CD_2Cl_2}$, (b) $\mathbf{1_2}\cdot\mathbf{4}$, (c) $\mathbf{1_2}\cdot\mathbf{2}$, (d) $\mathbf{1_2}\cdot\mathbf{3}$. The symbol ● denotes the solvent-filled capsule's N–H resonance.

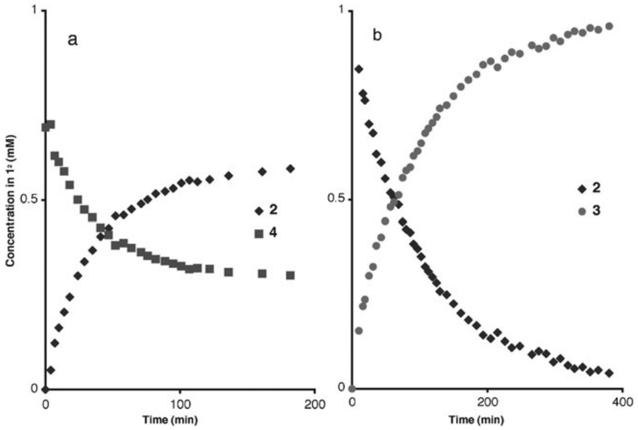

Fig. 4 Binding competition experiments of guests **2**, **3** and **4** for capsule $\mathbf{1_2}$ in $\mathrm{CD_2Cl_2}$, as monitored by ^{1}H NMR spectroscopy (1 mM) (see ESI‡).

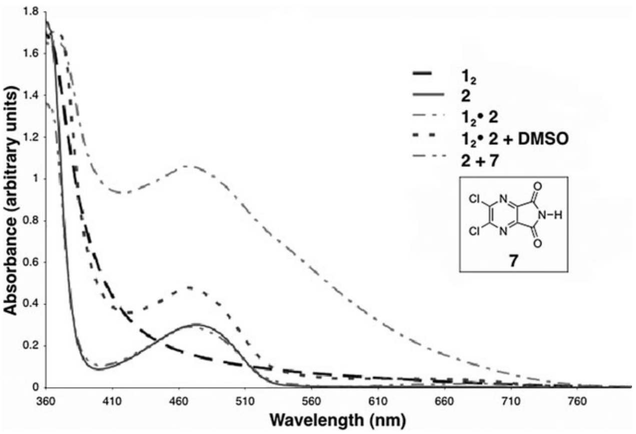

Fig. 5 UV-vis spectra highlighting long wavelength absorption of the $\mathbf{1_2}\cdot\mathbf{2}$ complex (1 mM in $\mathrm{CH_2Cl_2}$).

Electrochemical experiments on these novel TTF encapsulation complexes are under way and will be reported in a sequel.

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