ORGANIC LETTERS

2011
Vol. 13, No. 7
1770–1773

Encapsulation of Tetrathiafulvalene Inside a Dimeric Molecular Capsule

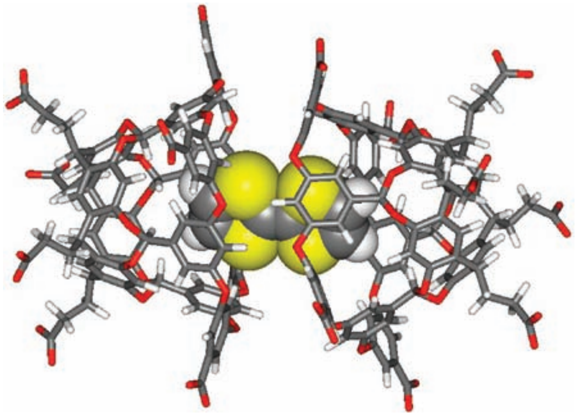
Yanhua Qiu, Song Yi, and Angel E. Kaifer*

Center for Supramolecular Science and Department of Chemistry, University of Miami, Coral Gables, Florida 33124-0431, United States

akaifer@miami.edu

Received February 1, 2011

ABSTRACT



Tetrathiafulvalene (TTF) is trapped inside a dimeric capsule formed by two octaacid, deep-cavity cavitands in aqueous solution. While the first one-electron oxidation of TTF is strongly hindered by encapsulation, the capsular assembly is eventually destabilized upon oxidation of the guest.

Tetrathiafulvalene (TTF) and its derivatives constitute an important class of compounds for the design and preparation of highly conducting organic solids.[1−4] TTF derivatives undergo two consecutive one-electron oxidations at very accessible potentials. This ease of oxidation has also led to their extensive utilization in switchable molecules.[5] Typically, TTF is oxidized to its cation radical (TTF^{+}) or dication (TTF^{2+}) forms so that the development of positive charge on the TTF residue triggers the electrostatic repulsion with other positively charged components, leading to a measurable effect.

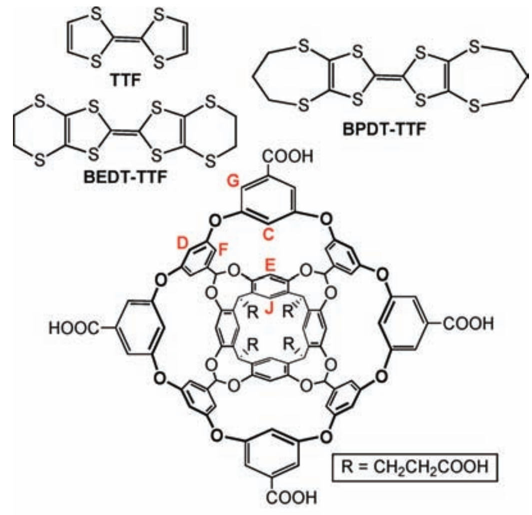
Gibb's octaacid[6] (compound **1** in Figure 1) is a deep-cavity cavitand with a well-defined "bowl" shape. Eight carboxylic acid groups on the outer surface of this cavitand increase its solubility to millimolar levels in basic aqueous solution. Under these conditions, octaacid cavitand **1** forms head-to-head dimeric molecular capsules in the presence of hydrophobic guests.[6,7] We have recently reported that ferrocene is included inside $\mathbf{1}_2$ molecular capsules in basic aqueous solution.[8] An intriguing result of this encapsulation is the loss of voltammetric response for the one-electron oxidation of ferrocene. Because of our long-standing interest on the electrochemical behavior or encapsulated redox centers,[9] we decided to extend our investigation to TTF as an interesting candidate for encapsulation by dimeric capsules of **1**.

We started our investigation by examining ^{1}H NMR spectroscopic data of host **1** in the presence of variable amounts of TTF. The experimental data are shown in Figure 2. The spectrum of host **1** shows the anticipated signals that have already been described in the literature. As TTF is added, a new set of peaks for the host protons

---

(1) Bryce, M. R. *J. Mater. Chem.* **2000**, *10*, 589.
(2) Martín, N.; Segura, J.-L. *Angew. Chem., Int. Ed.* **2001**, *40*, 1372.
(3) Yamada, J; Sugimoto, T. *TTF Chemistry: Fundamentals and Applications of Tetrathiafulvalene*; Kodansha (Tokyo) and Springer: New York, 2004.
(4) Batail, P. *Chem. Rev.* **2004**, *104*, 4887.
(5) Canevet, D.; Sallé, M.; Zhang, G.; Zhang, D.; Zhu, D. *Chem. Commun.* **2009**, 2245.
(6) Gibb, C. L. D.; Gibb, B. C. *J. Am. Chem. Soc.* **2004**, *126*, 11408.
(7) Jayaraj, N.; Zhao, Y.; Parthasarathy, A.; Porel, M.; Liu, R. S. H.; Ramamurthy, V. *Langmuir* **2009**, *25*, 10575.
(8) Podkoscielny, D.; Philip, I.; Gibb, C. L. D.; Gibb, B. C.; Kaifer, A. E. *Chem.—Eur. J.* **2008**, *14*, 4704.
(9) Gadde, S.; Batchelor, E. K.; Kaifer, A. E. *Aust. J. Chem.* **2010**, *63*, 184.

10.1021/ol200258g



1

Figure 1. Structures of the guests (TTF derivatives) and the host (octaacid cavitand **1**) used in this work.

appears and grows at the expense of the original peaks. In particular, the "D" protons (see Figure 1 for proton labels) undergo a pronounced downfield shift in the presence of TTF, but all aromatic protons are affected. Once the TTF concentration reaches the 0.5 equiv mark, further additions of TTF no longer have any significant effect on the spectra. This finding is consistent with the anticipated stoichiometry for the inclusion of TTF inside a dimeric molecular capsule (an assembly that we will denote as TTF@$\mathbf{1}_2$).

TTF is a very hydrophobic compound, and its aqueous solubility is well below the millimolar concentrations used in the ^{1}H NMR experiments.[10] The fact that we can dissolve TTF at a concentration of 1 mM in an aqueous solution containing 2 mM of host **1** is by itself a strong indication that there is an efficient binding interaction between the two compounds. In the NMR experiments of Figure 2, additions of up to 0.5 equiv of TTF result in perfectly transparent solutions. However, once the total amount of added TTF exceeds 0.5 equiv, the solutions become turbid, because the amount of host is not enough to bind and solubilize all the TTF added. Figure 3 shows two pictures taken to illustrate the completely different appearance of solutions with fully dissolved TTF (in the presence of **1**) and undissolved TTF guest (in the absence of **1**).

All these observations strongly suggest the encapsulation of TTF inside a $\mathbf{1}_2$ dimeric capsule. To confirm this point, we carried out diffusion coefficient measurements using pulse gradient spin echo (PGSE) NMR techniques.[11] The diffusion coefficient (D_o) was measured as $(1.95 \pm 0.05) \times 10^{-6}$ cm^2/s for free cavitand **1** and $(1.45 \pm 0.05) \times 10^{-6}$ cm^2/s for cavitand **1** in the presence of 0.5 equiv of TTF. Further additions of TTF did not change the D_o value but led to turbid solutions as discussed before. The diffusion coefficients measured here are about 10% smaller than the values that we had reported before for monomeric **1** and guest@$\mathbf{1}_2$ capsules,[8] a difference that we believed is due to calibration problems in our previous measurements. The values reported in this work are similar to other values reported for this cavitand[7] and strongly support the formation of the dimeric molecular capsules containing trapped TTF as the hydrophobic guest driving the formation of the assembly (TTF@$\mathbf{1}_2$).

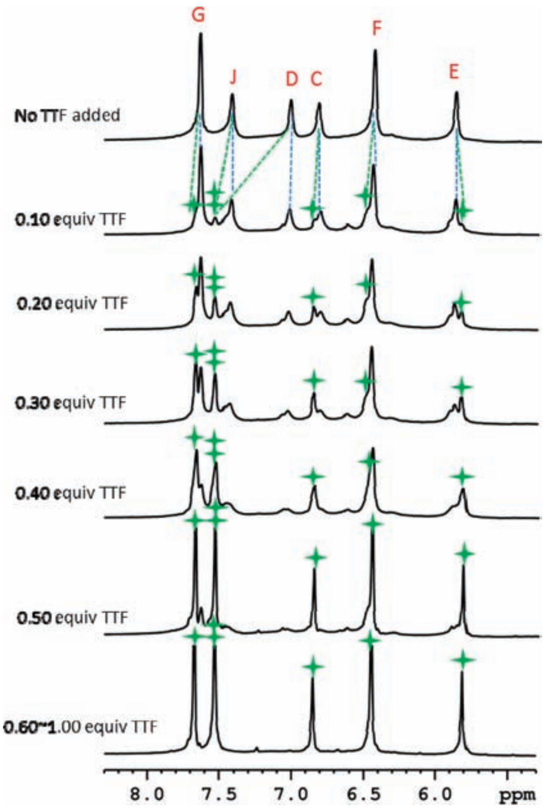


Figure 2. Aromatic section of the ^{1}H NMR spectra (500 MHz 10 mM borate buffer pH 8.9 in D$_2$O) of host **1** (1 mM) in the presence of increasing concentrations of TTF. Proton resonances labeled with a "cross" correspond to complexed **1**.

As mentioned above, TTF and its derivatives undergo two consecutive one-electron oxidations to first generate a cation radical (TTF$^+$) and eventually a dication (TTF^{2+}) at more positive potentials. In organic solvents, where TTF is sufficiently soluble, the electrochemical behavior shows the expected two sets of waves corresponding to the two reversible processes[5] ($\mathrm{TTF} \rightleftarrows \mathrm{TTF}^{+} + \mathrm{e}^{-}$ and $\mathrm{TTF}^{+} \rightleftarrows \mathrm{TTF}^{2+} + \mathrm{e}^{-}$). In aqueous solution, the first oxidation is poorly developed because of the low solubility of TTF, but the second oxidation gives rise to a larger wave as the charged, oxidized TTF forms are considerably more soluble.[12,13] Therefore, we set out to record the

---

[10] Leheny, A. R.; Rossetti, R.; Brus, L. E. *J. Phys. Chem.* **1985**, *89*, 211.

[11] Cohen, Y.; Avram, L.; Frish, L. *Angew. Chem., Int. Ed.* **2005**, *44*, 520.

[12] Eddowes, M. J.; Grätzel, M. *J. Electroanal. Chem.* **1983**, *152*, 143.

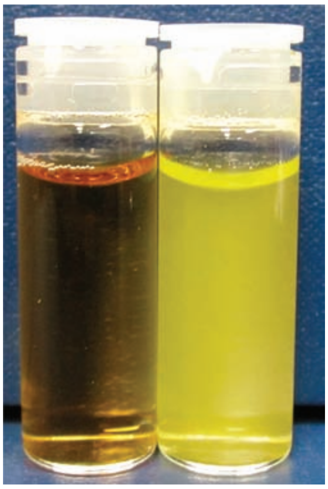


Figure 3. Both solutions contain 1.0 mM TTF + 20 mM borate buffer pH 8.9 in water. Left vial: 2.0 mM host **1** added to solubilize TTF. Right vial: no host **1** added.

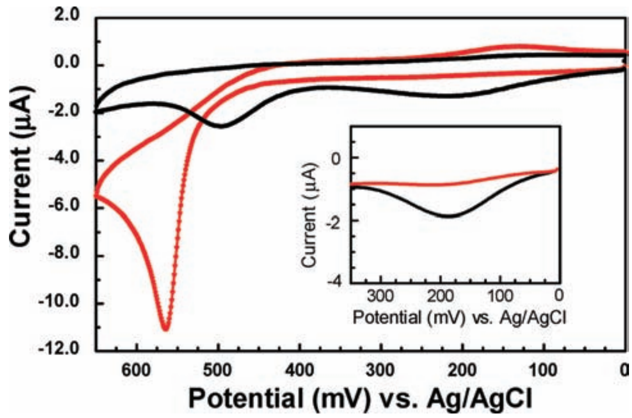


Figure 4. CV responses on glassy carbon (0.07 cm^2) of a saturated TTF aqueous solution (black trace) also containing 50 mM NaCl and 10 mM borate buffer pH 8.9 and a 0.5 mM TTF + 1.0 mM **1** solution (red trace) in the same aqueous medium. Scan rate: 0.1 V s^{-1}. The insert shows the SWV responses of the same two solutions in the potential range associated with the first TTF oxidation.

electrochemical behavior of TTF trapped inside the $\mathbf{1}_2$ capsule using cyclic voltammetry (CV). The experimental results are shown in Figure 4. The black trace depicts the voltammetric behavior in the absence of host **1**, showing the poorly developed anodic wave for the TTF → $TTF^+ + e^-$ oxidation process centered at +0.18 V vs Ag/AgCl. The second anodic wave (at +0.48 V) exhibits a higher current level, but no peaks are observed on the reverse scan, suggesting the fast disappearance of the dication. In the presence of 2.0 equiv of host **1** (red trace), the small anodic current for the first oxidation process disappears, in spite of the fact that the effective concentration of TTF in this solution is 0.5 mM (with the TTF molecules encapsulated inside $\mathbf{1}_2$ assemblies). We have reported very similar results for encapsulated ferrocene (Fc); that is, the Fc@$\mathbf{1}_2$ assembly was found to be voltammetrically silent in the potential region corresponding to Fc oxidation.[8] As the CV potential scan with TTF@$\mathbf{1}_2$ extends to more positive values, a well-defined wave was recorded in the potential region corresponding to the second oxidation process (at +0.56 V) and a small peak was observed on the reverse scan at potentials associated with the $TTF^+ + e^- \rightarrow TTF$ reduction process.

In order to confirm that the first one-electron oxidation of TTF is shut off upon encapsulation, we carried out voltammetric experiments using square wave voltammetry (SWV), a technique that has inherently better sensitivity than CV. In the absence of host **1**, we observed a small peak for the oxidation of the low concentration of TTF that results from its limited aqueous solubility (see insert in Figure 4). However, in the presence of 2.0 equiv of **1**, a 0.5 mM concentration of the TTF@$\mathbf{1}_2$ assembly is present in the solution, but the SWV trace fails to reveal any significant faradaic current levels. Clearly, this result constitutes strong evidence for the hindered voltammetric response of encapsulated TTF.

The observed hindrance for the electron-transfer process from the guest (in TTF@$\mathbf{1}_2$) to the electrode is probably due to very slow electrochemical kinetics, resulting from the increased distance between encapsulated TTF (compared to free TTF) and the electrode surface. We have used similar arguments to explain the lack of voltammetric response observed with the Fc@$\mathbf{1}_2$ assembly.[8] However, oxidation of encapsulated Fc in the latter assembly can be accomplished using a cationic mediator,[14] which attaches itself quite strongly to the negatively charged surface of the $\mathbf{1}_2$ capsule. In that case, oxidation of the guest leads to dissociation of the molecular assembly because the oxidized Fc^+ species is less hydrophobic than the neutral guest and does not serve as an effective molecular "glue" to keep the assembly together. In the case investigated here, slow oxidation of TTF@$\mathbf{1}_2$ seems to take place, eventually leading to the observation of the TTF^+ oxidation wave.[15] However, the fact that the peak potential for this anodic wave is more positive than that observed for the same oxidation in the absence of host **1** is consistent with the release of TTF^+ from the capsule. Furthermore, although the dicationic species (TTF^{2+}) decomposes rapidly under the basic pH conditions of our experiments, the reduction of a small amount of free TTF^+ is observed in the reverse scan. All these observations clearly indicate that the slow electrochemical oxidation of TTF@$\mathbf{1}_2$ leads to the disassembly of the molecular capsule and the release of the less hydrophobic oxidized guest.

---

(13) Yoshizawa, M.; Kumazawa, K.; Fujita, M. *J. Am. Chem. Soc.* **2005**, *127*, 13456.

(14) Podkoscielny, D.; Gadde, S.; Kaifer, A. E. *J. Am. Chem. Soc.* **2009**, *131*, 12876.

(15) A considerably larger current is expected from the voltammetric oxidation of TTF^+ than from the oxidation of TTF@$\mathbf{1}_2$, as the latter species has a much lower diffusion coefficient.

The oxidation of encapsulated TTF is quite slow but still allows the eventual observation of a more developed wave for the oxidation of TTF^+.[15] This wave may also include faradaic components resulting from the kinetically hindered oxidation of TTF. The relatively loose fitting of TTF inside the $\mathbf{1}_2$ capsule may weaken the overall stability of the supramolecular assembly. The hypothesis that TTF fits loosely inside the inner space of the capsule is consistent with the lack of observation of an NMR resonance for the TTF protons in the assembly TTF@$\mathbf{1}_2$. This signal is likely to be broadened by the exchange of the trapped guest among several possible locations inside the capsule. In contrast to this the bulkier ferrocene shows a relatively sharp resonance for its protons in the Fc@$\mathbf{1}_2$ assembly.[8]

Because of their importance in the research area of conducting organic solids, we also carried out experiments with two bulkier and more hydrophobic TTF derivatives, bis(ethylenedithio)tetrathiafulvalene and bis(propylenedithio)tetrathiafulvalene (BEDT-TTF and BPDT-TTF, see structures in Figure 1). However, all our attempts to solubilize these TTF derivatives in aqueous solutions containing host **1** failed,[16] preventing further experimentation with these guests. Two reasons can be put forward to rationalize the failure of these guests to drive the formation of $\mathbf{1}_2$ capsules around them. First, these TTF derivatives are considerably more hydrophobic than TTF itself, which limits their aqueous solubility to even lower values and, thus, thwarts their binding interactions with host **1**. Second, both guests have larger molecular volumes than TTF, which restricts their inclusion in the cavity of the $\mathbf{1}_2$ dimeric capsules. We have done some preliminary molecular modeling computations on these molecular assemblies and the results suggest that each of these guests is bulky enough to prevent the hydrophobic head-to-head closing of the dimeric molecular capsules around them (see the Supporting Information).

In conclusion, we have demonstrated here that TTF is encapsulated inside a molecular capsule formed by the head-to-head assembly of two molecules of octaacid, deep-cavity cavitand **1** in basic aqueous solution. The voltammetric response of TTF@$\mathbf{1}_2$ is strongly hindered, although slow oxidation of encapsulated TTF leads to the disruption of the molecular assembly. These results constitute an excellent example of two complementary phenomena. First, supramolecular structures can exert strong effects on the kinetics of heterogeneous electron transfer reactions. Second, electron-transfer reactions can be used to effectively destroy or disrupt supramolecular assemblies.

Acknowledgment. We are grateful to the National Science Foundation (to A.E.K., CHE-848637) for financial support of this research. We acknowledge Dr. Dagmara Podkoscielny (University of Miami) for carrying out preliminary experiments and Dr. Simin Liu (University of New Orleans) for helpful synthetic advice.

Supporting Information Available. Additional voltammetric and computational data as mentioned in the text. This material is available free of charge via the Internet at http://pubs.acs.org.

---

(16) To a solution containing 2.0 mM host **1** in 10 mM borate buffer was added a solid amount of BEDT−TTF (enough to make its concentration 1.0 mM). The mixture was warmed at 60 °C and sonicated for 30 min. Undissolved solid BEDT−TTF was recovered by filtration after the procedure.