

Tetra-TTF Calix[4]pyrrole: A Rationally Designed Receptor for Electron-Deficient Neutral Guests

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Considerable effort has been focused on the preparation of supramolecular host systems with the capability of recognizing specific chemical species through weak, noncovalent interactions.¹ The incorporation of redox-active components into host molecules is one means of enhancing the guest recognition process via, e.g., increased donor–acceptor interactions. In this context, the use of tetrathiafulvalene² (TTF) appears particularly attractive. To date, a number of TTF-containing systems have been synthesized to study host–guest binding events.^{2,3} However, in almost all cases only weak interactions were observed with neutral guests.

Herein, we report the synthesis of the first tetra-TTF calix[4]pyrrole **2**. This system acts as an effective receptor for neutral electron acceptors, such as 1,3,5-trinitrobenzene (**3**), tetrafluoro-*p*-benzoquinone (**4**), tetrachloro-*p*-benzoquinone (**5**), and *p*-benzoquinone (**6**), in CH₂Cl₂ solution and in the case of **3**, **4**, and Me₂CO, also in the solid state. This neutral substrate recognition process can be blocked by the addition of chloride anion. Prior to this work, few reports of neutral substrate binding by calix[4]pyrroles had appeared.⁴ System **2** has been designed to take advantage of the fact that calix[4]pyrroles generally exist in the 1,3-alternate conformation in the absence of anions.⁵ In this conformation, each pair of identical TTF electron donors is expected to hold an electron-deficient guest in a sandwichlike fashion via charge transfer (CT) interactions. Additional stabilization is also expected to be provided by the pyrrole NH hydrogen bond donors.

The synthesis of the tetra-TTF calix[4]pyrrole **2** is outlined in Scheme 1. Treating the monopyrrolo-TTF⁶ **1** with an excess of TFA in a mixture of CH₂Cl₂ and Me₂CO gave the tetra-TTF calix[4]pyrrole **2** as a yellow solid in 18% yield. It was fully characterized (cf. Supporting Information).

Initial evidence for the interaction between **2** and **3** came from X-ray crystallography. Diffraction-grade crystals were grown by slow diffusion of a pentane layer into a CH₂Cl₂ solution containing **2** and **3** in a 1:2 ratio. The resulting structural analysis (Figure 1) revealed a solid-state structure containing two different tetra-TTF calix[4]pyrrole **2** units. Each of these complexes contains two guest molecules (**3**) sandwiched between each pair of TTF “arms”, thus forming two different 1:2 CT complexes. In the first of these complexes, the guest molecules **3** have two of their nitro groups pointing toward the NH protons and are involved in hydrogen-bonding interactions in the solid state. In the second complex, one guest molecule has two of its nitro groups oriented toward the NH protons, whereas the second guest has only one nitro group oriented toward the NH protons. In both of these complexes, the interplanar distance between pairs of TTFs is in the range of 6.80–7.10 Å.⁷ Single-crystal X-ray diffraction structures of the 1:2 complexes

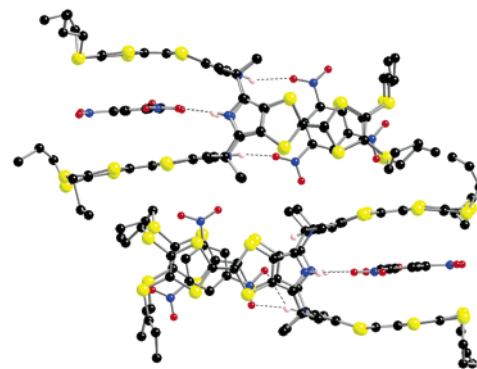
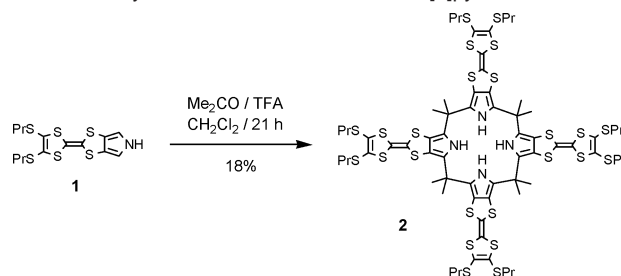


Figure 1. View illustrating the H-bonding interactions (dashed lines) between **2** and **3** in the 1:2 complex **2**·(**3**)₂.

Scheme 1. Synthesis of the Tetra-TTF Calix[4]pyrrole **2**



between **2** and Me₂CO and between **2** and **4** were also obtained and found to be similar to that of **2**·(**3**)₂ (cf. Supporting Information).

The interactions between host **2** and the electron-deficient guests **3**–**6** were studied in CH₂Cl₂ solution using UV–vis spectroscopy. None of these substrates gave rise to any notable visible absorption bands at $\lambda \geq 500$ nm. Addition of 2 equiv of **3** to a CH₂Cl₂ solution of **2** resulted in an immediate color change from yellow to green and the appearance (see Figure 2) of a CT absorption band centered at $\lambda = 677$ nm ($\epsilon = 477$ M⁻¹ cm⁻¹) in the UV–vis spectrum. This observation is thought to reflect the presence of CT interactions between the donor and the acceptor units present in **2** and **3**, respectively.

Addition of an anion to calix[4]pyrrole shifted the equilibrium from the 1,3-alternate to the corresponding cone conformation.⁵ Addition of 5 equiv of tetrabutylammonium chloride (TBACl) to a CH₂Cl₂ solution containing **2**·(**3**)₂ gave rise to a color change from green back to yellow and the disappearance (Figure 2) of the CT absorption band centered at $\lambda = 677$ nm in the UV–vis spectrum. Addition of chloride ions to the solution of **2**·(**3**)₂ resulted in a competition between the chloride ions and the electron-deficient guests for hydrogen-bonding interactions with the NH protons of

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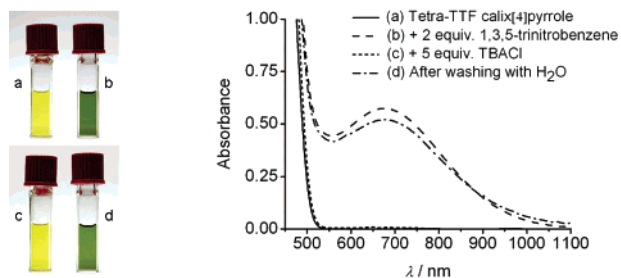
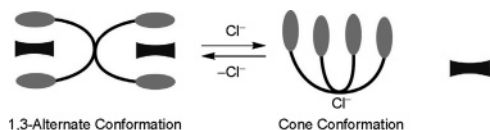


Figure 2. Absorption spectra (CH_2Cl_2 , 25 °C) of (a) **2** (1.0 mM), (b) **2** + 2 equiv of **3**, (c) **2** + 2 equiv of **3** + 5 equiv of TBACl, and (d) after washing with H_2O .

Scheme 2. Cartoon Representation Illustrating the Change in Conformation Associated with the Addition/Removal of Chloride Anion to a CH_2Cl_2 Solution of the Tetra-TTF Calix[4]pyrrole **2** and the Electron-Deficient Guest **3** (represented by the distorted rectangle)^a



^a The shaded ellipse is meant to denote the TTF substituents on the β -pyrrolic positions of the calix[4]pyrrole.

2 and therefore a competition between the 1,3-alternate conformation and the cone conformation. However, because of the high binding constant between **2** and chloride ions,⁸ the equilibrium was largely shifted in favor of the cone conformation. This, in turn, led to the release (Scheme 2) of the electron-deficient guest **3** since the cavities present in **2** in its 1,3-alternate conformation were no longer available for binding. Extracting the TBACl salt from the organic CH_2Cl_2 phase by washing with H_2O regenerated the CT complex $2 \cdot (3)_2$, and as a consequence, the green color of the CH_2Cl_2 solution was reestablished. Addition of 2 equiv of **4**, **5**, or **6** to a CH_2Cl_2 solution of **2** also resulted in an immediate color change, an effect that was reversed upon addition of chloride ions. Presumably, the formation of the host–guest complex $2 \cdot (3)_2$ in the absence of anions is enhanced by hydrogen-bonding interactions between two NH protons from the host **2** and one or two of the nitro groups present in guest **3**. Support for this hypothesis is evident from ^1H NMR spectroscopic analyses. For instance, the ^1H NMR spectrum (CDCl_3 , 298 K) of **2** reveals a signal resonating at $\delta = 7.10$ ppm, which is assigned to the free NH protons. Upon addition of two equiv of **3** to this solution, the signals corresponding to the resonances of the NH protons are shifted to $\delta = 7.79$ ppm ($\Delta\delta = +0.69$ ppm) as a result of hydrogen-bonding interactions to the guest(s). In this mixture, the CH protons of **3** are, presumably as a consequence of being sandwiched between two shielding TTF subunits, found to resonate at $\delta = 9.20$ ppm ($\Delta\delta = -0.17$ ppm relative to their initial position at $\delta = 9.37$ ppm). Upon addition of 5 equiv of TBACl, the CH resonance in **3** is observed essentially at its initial position ($\delta = 9.35$ ppm).

Upon release of the guest(s) on the other hand, the NH protons of **2** are shifted further downfield ($\delta = 10.80$ ppm) as a result of hydrogen-bonding interactions occurring between the NH protons and the chloride ion.

A continuous-variation ^1H NMR experiment (Job plot) was carried out and found to exhibit a maximum at a molar fraction of

approximately 0.6, thus indicating that **2** forms a 1:2 complex with **3**. A similar stoichiometry was seen between **2** and **4**. Monitoring the changes in the chemical shift for the signal associated with the NH protons upon the addition of increasing amounts of **3** or **4** to the receptor **2** at 298 K, allowed the associated binding constants to be determined (see Supporting Information). For **3** and **4** the first binding constant is low ($K_1 = 20 \text{ M}^{-1}$ in both cases) compared to the second binding constant ($K_2 = 900$ and 3500 M^{-1} for **3** and **4**, respectively). This is consistent with a change in geometry of **2** being caused by the binding of a first guest that presumably results in a better fit for the second guest. The binding constants for **5** and **6** were low, being ca. 60 and 40 M^{-1} , respectively.

In conclusion, we have demonstrated the first example of a calix-[4]pyrrole incorporating four appended TTF units. This calix[4]-pyrrole acts as a sandwichlike host molecule for electron-deficient guests in its 1,3-alternate conformation. Addition of chloride ions, however, serves to effect release of these guests. The dynamic nature of receptor **2** makes it a potentially versatile scaffold for studying donor and acceptor interactions between TTF and planar electron-deficient guests within a well-defined unimolecular system. Tests of this possibility are underway using a variety of methods, including electrochemical means.

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Supporting Information Available: Synthesis and characterization data for **2**, a list of binding profiles for NMR titrations between host **2** and guests **3**, **4**, **5**, and **6**, Job plots between host **2** and guests **3**, and **4**, and X-ray experimental details for $2 \cdot (\text{Me}_2\text{O})_2$, $2 \cdot (3)_2$, and for $2 \cdot (4)_2$ in CIF format This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (7) The distance between the two TTF subunits in question is the distance between the central fulvalene bonds.
- (8) The binding constant K_a between **2** and Cl^- ions was measured by isothermal calorimetry (ITC) in $\text{CH}_2\text{ClCH}_2\text{Cl}$ and CH_2Cl_2 , respectively. In the case of $\text{CH}_2\text{ClCH}_2\text{Cl}$ a value of ca. $2.5 \times 10^6 \text{ M}^{-1}$ was obtained. However, the use of CH_2Cl_2 as solvent did not give reliable results. **2** was not soluble in more polar solvents, such as Me_2SO and MeCN, and therefore no binding studies between **2** and Cl^- ions have been conducted in these solvents.

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