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An investigation of the role of the disparate redox states of the tetrathiafulvalene unit in modulating hydrogen bonding interactions in solution

Alan S. F. Boyd,[a] Graeme Cooke,[a,*] Florence M. A. Duclairoir[a] and Vincent M. Rotello[b]

[a]*The Centre for Biomimetic Design and Synthesis, Department of Chemistry, William H. Perkin Building, School of Engineering and Physical Sciences, Heriot-Watt University, Riccarton, Edinburgh EH14 4AS, UK*
[b]*Department of Chemistry, University of Massachusetts at Amherst, Amherst, MA 01002, USA*

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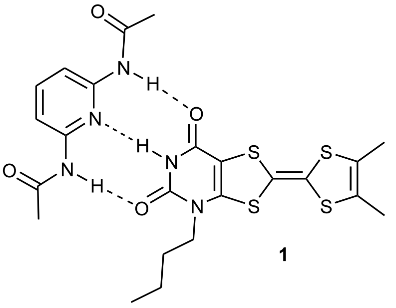
Abstract—We have investigated the electrochemically controlled hydrogen bonding interactions between tetrathiafulvalene host **3** and guests **4** or **5**. Stabilisation of the $\mathbf{3}^{+\bullet}$ state is dependent upon the nature of the guest species, whereas both guests prevent precipitation of the electrochemically generated $\mathbf{3}^{2+}$ species at the working electrode via hydrogen bonded molecular recognition processes. © 2002 Elsevier Science Ltd. All rights reserved.

The application of electrochemistry to modulate hydrogen bonding interactions between host–guest complexes is an important field within supramolecular chemistry.[1] In particular, the electrochemically controlled gain or loss of an electron by a redox active host (or guest) can profoundly influence the electrostatic interactions between a hydrogen bonded host–guest dyad, leading to major changes in the strength of the intermolecular interactions between these units.[2] Therefore, it is remarkable that the tetrathiafulvalene (TTF) unit with its multi-stable oxidation states (TTF^0, $\mathrm{TTF}^{+\bullet}$, TTF^{2+}), has not been more widely incorporated into electrochemically controllable hydrogen bonded motifs.[3] The electrochemically controlled hydrogen bond complexation between dimethyl-[1-butyl-2,4-dioxo-(1*H*,3*H*)pyrimido]-TTF **1** and 2,6-di(*N*-acetylamino)pyridine **2** has recently been reported.[4] This study revealed that the radical cation state of **1** was anodically shifted by +30 mV upon complex formation with **2**, showing that a 3–4-fold decrease in the stability of the complex occurred. However, determining the role of the dicationic state of **1** in the electrochemically controlled recognition process was hampered by the complexity of this redox wave. Here, we report the electrochemically controlled recognition between a pyridyl–TTF host **3** and complementary guests **4** and **5**.[5] The non-fused nature of the pyridine recognition unit and the TTF signalling unit of **3** provides a host with well-defined oxidation waves, allowing the role of the radical cation and dicationic states in molecular recognition to be probed.

The TTF host **3** was synthesised by reacting 2-amino-6-methylpyridine with 1 equiv. of 4-chlorocarbonyl-TTF[6] in CH_2Cl_2 in the presence of triethylamine. Compound



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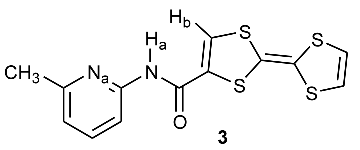

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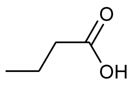

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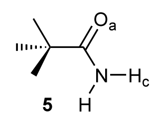

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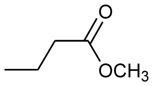

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Keywords: tetrathiafulvalene; recognition; electrochemistry.

* Corresponding author. Tel.: 0131 451 8184; fax: 0131 451 3180; e-mail: g.cooke@hw.ac.uk

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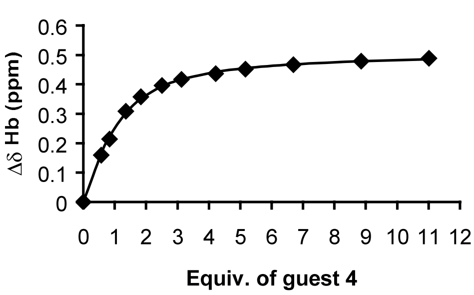

Figure 1. Plot of Δδ for proton H_b of **3** versus equivalents of guest **4** added.

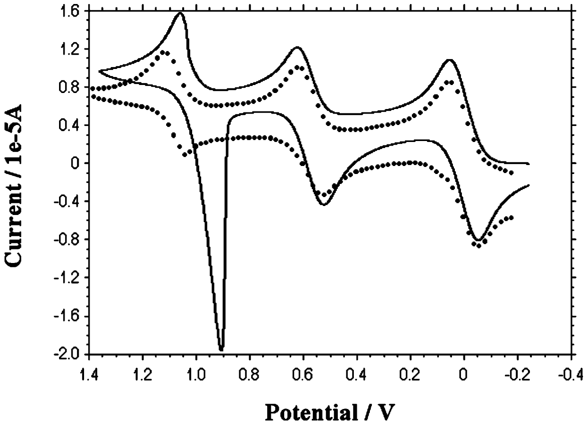

Figure 2. Cyclic voltammograms of a 10^{-3} M solution of host **3** (solid line) and in the presence of excess (10^{-2} M) **4** (dotted line).

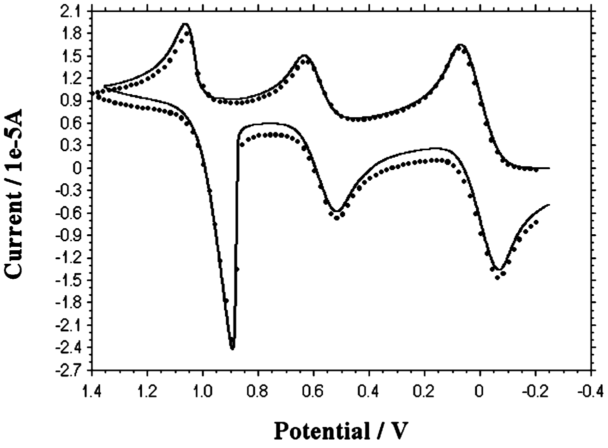

Figure 3. Cyclic voltammograms of a 10^{-3} M solution of host **3** (solid line) and in the presence of excess (10^{-2} M) **6** (dotted line).

3 was readily purified using column chromatography to afford the host unit in 65% yield.[7] Hydrogen bond formation between **3** and **4** was confirmed by changes in the ^{1}H NMR spectra of host **3**. Addition of aliquots of guest **4** to a solution of host **3** in $CDCl_3$ resulted in smooth downfield shifts of the resonances of H_a and H_b. The shift in the latter indicates that this TTF proton is sufficiently acidic to be involved in hydrogen bonding processes (Fig. 1). The NMR data were fit to a 1:1 binding isotherm, providing an association constant (K_a) for **3·4** of 390 (±20) M^{-1} (based upon the shift H_b).[2f] Hydrogen bond formation was also observed between **3** and **5**, however, much smaller shifts in the resonances of H_a and H_b were observed upon the addition of **5**, leading to an estimated association constant of <1 M^{-1}. This low association constant is presumably due to the competing strong dimerisation of **5** in chlorinated solvents.

With host–guest complexation verified for **3·4** and **3·5**, we next investigated the electrochemically modulated binding properties of these systems using cyclic (CV) and square-wave (SWV) voltammetry studies.[8] CV studies performed on compound **3** gave rise to a reversible single electron oxidation wave for the formation of the $\mathbf{3}^{+\bullet}$ species ($E^1_{1/2} = +0.57$ V) and an irreversible single electron oxidation wave for the formation of the $\mathbf{3}^{2+}$ species centred around +0.99 V (Fig. 2). Although the irreversible nature of the oxidation wave for the $\mathbf{3}^{2+}$ state prevents meaningful quantitative investigation of its binding efficiency to complementary guests, this redox wave is considerably more defined than that obtained for **1**, and thus can provide qualitative information regarding the role of the $\mathbf{3}^{2+}$ state in modulating guest recognition.

The addition of excess **4** to a solution of **3** did not affect the oxidation wave for the $\mathbf{3}^{+\bullet}$ state. However, the wave for the $\mathbf{3}^{2+}$ state now becomes reversible, which indicates that host–guest complexation prevents precipitation of the $\mathbf{3}^{2+}$ species at the working electrode surface.[9] In order to confirm that molecular recognition between **4** and the $\mathbf{3}^{2+}$ is responsible for the formation of the reversible redox wave, we investigated the electrochemistry of **3** upon the addition of an excess of related guest **6**, where effective recognition cannot occur. The cyclic voltammogram of **3** was essentially unchanged upon the addition of an excess of **6**, and in particular, the oxidation wave for the $\mathbf{3}^{2+}$ state remains irreversible (Fig. 3). Thus, the data are consistent with molecular recognition between **3** and **4** being responsible for preventing precipitation of the $\mathbf{3}^{2+}$ at the working electrode.

When the CVs or SWVs of host **3** were recorded following the addition of an excess of guest **5**, a −33 mV shift in the half-wave potential for the $\mathbf{3}^{+\bullet}$ species was observed, indicating a stabilisation (3.18 kJ mol^{-1}) of the radical cationic state of receptor **3**, and hence corresponds to guest **5** becoming more strongly bound to **3** (Fig. 4). The CV data are in contrast to those obtained with guest **4**, and indicate that redox controlled recognition properties of **3** are dependent upon the nature of the guest. In accordance with the electrochemical data obtained with guest **4**, the addition of guest **5** to **3** resulted in the formation of a reversible oxidation wave for the $\mathbf{3}^{2+}$ state.

It is apparent from our experimental data that the role of the radical cation state of **3** in modulating hydrogen bonding is dependent upon the nature of the complementary guest. To probe the influence of the TTF unit's oxidation states in modulating the properties of the donor/acceptor sites of the hydrogen bonding surface of **3**, we have calculated the electrostatic potentials (ESP) for the atoms of the host in its different oxidation states ($\mathbf{3^{0}}$, $\mathbf{3^{+\bullet}}$, $\mathbf{3^{2+}}$) and the results are summarised in Table 1.[10] The calculated values for the ESP of N_a for receptors $\mathbf{3^{0}}$, $\mathbf{3^{+\bullet}}$ and $\mathbf{3^{2+}}$ revealed a small sequential decrease in the negative ESP, which is consistent with the oxidised electron deficient TTF unit removing electron density from the pyridyl-nitrogen. Interestingly, the ESP of H_a was identical for the $\mathbf{3^{0}}$ and $\mathbf{3^{+\bullet}}$ states, however, a small positive increase in ESP was observed for the $\mathbf{3^{2+}}$ state. Conversely, proton H_b shows markedly differing behaviour to that of H_a, as the ESP of this atom displays an increase in positive ESP for the $\mathbf{3^{+\bullet}}$ and $\mathbf{3^{2+}}$ states compared to the neutral host.

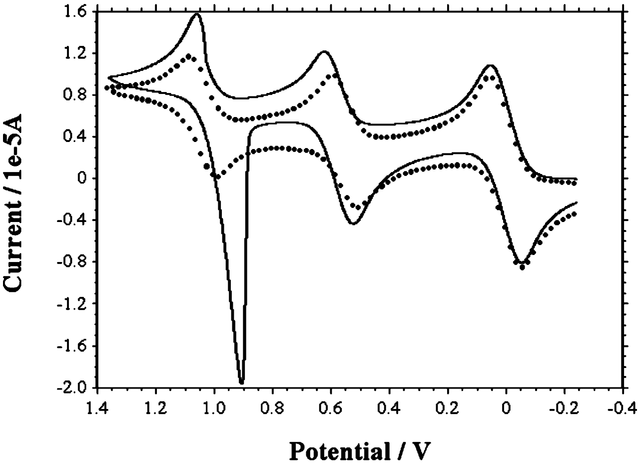

Figure 4. Cyclic voltammograms of a 10^{-3} M solution of host **3** (solid line) and in the presence of excess **5** (10^{-2} M) (dotted line).

Table 1. Calculated charges fitted to ESP for selected atoms (6-311G* B3LYP-DFT//3-21G* UHF)

Atom	**3**	$\mathbf{3^{+\bullet}}$	$\mathbf{3^{2+}}$	**3·5**	$\mathbf{3^{+\bullet}}$**·5**
Pyridyl N_a	−0.72	−0.71	−0.70	−0.73	−0.73
H_a	+0.31	+0.31	+0.34	+0.46	+0.50
H_b	+0.25	+0.29	+0.29	+0.34	+0.30
H_c				+0.59	+0.59
O_a				−0.78	−0.80

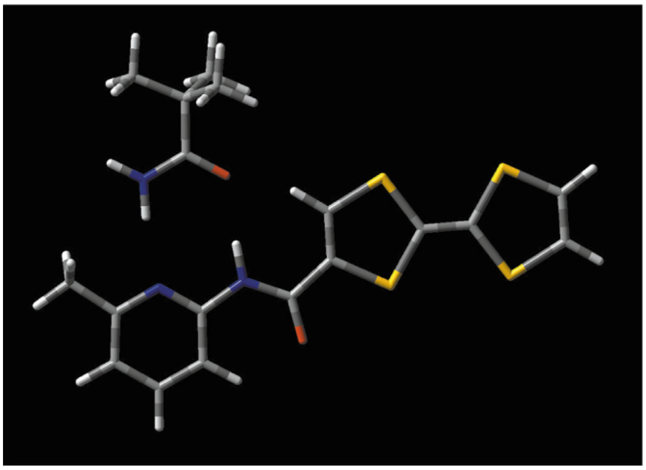

Figure 5. Modelled structure (UHF 3-21G*) of **3·5**.

We have modelled complex **3·5** and $\mathbf{3^{+\bullet}}$**·5** in order to investigate the role of the $\mathbf{3^{+\bullet}}$ in modulating the hydrogen bonding efficiency between the host–guest dyad. In both cases the modelled structures predict hydrogen bond formation between $N_a \cdots H_c$ and $O_a \cdots H_a(H_b)$ (Fig. 5). Upon complexation with **5**, little change was observed for the ESP of N_a, however, a significant increase in the positive ESP of H_a ($\Delta = +0.15$) and to a lesser extent, H_b ($\Delta = +0.09$) was observed. The ESP of N_a and H_c in $\mathbf{3^{+\bullet}}$**·5** are essentially unchanged from those obtained for **3·5**, indicating that hydrogen bonding between these atoms is not significantly altered upon the formation of the $\mathbf{3^{+\bullet}}$ species. However, more pronounced changes are observed in the ESP of H_a ($\Delta = +0.04$), H_b ($\Delta = -0.04$) and O_a ($\Delta = -0.02$), indicating that the increased stability of the $\mathbf{3^{+\bullet}}$**·5** complex is likely to be due to the redox induced changes in polarizability of the $O_a \cdots H_a(H_b)$ hydrogen bonds.

In conclusion, we have shown that the nature of the guest has an important role in the electrochemically controlled hydrogen bond formation between host **3** and guests **4** or **5**. Oxidation of $\mathbf{3^{0}}$ to $\mathbf{3^{+\bullet}}$ state has no effect on the hydrogen bonding efficiency with **4**, however, when guest **5** was studied, a 3.18 kJ mol^{-1} stabilisation of the complex was observed for the same redox process. The CV data following the addition of either guest are consistent with molecular recognition processes preventing precipitation of the $\mathbf{3^{2+}}$ species at the working electrode. Experiments are underway in our laboratory to synthesise TTF-based receptors with reversible oxidation waves for their dicationic states in order that the precise role of this moiety in hydrogen bonded processes can be quantified, and the results from these experiments will be reported in due course.

Acknowledgements

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5. Compound **5** was utilised rather than the corresponding *n*-butylamide derivative, due to the better solubility of the former in CH_2Cl_2 or $CDCl_3$. However, similar shifts in the half-wave potentials of the CV of **3** were observed regardless of which amide guest was added.
6. Panetta, C. A.; Baghdadchi, J.; Metzger, R. *Mol. Cryst. Liq. Cryst.* **1984**, *107*, 103.
7. *Selected data for* **3**: Yield 65%, mp 171–173°C; Calculated for $C_{13}H_{10}N_2OS_4$: C, 46.15; H, 2.98; N, 8.33. Found: C, 46.25; H, 2.97; N, 8.37. ^{1}H NMR (400 MHz, $CO(CD_3)_2$, TMS): δ 2.38 (s, 3H), 6.65 (2d (AB), 2H), 6.98 (d, 1H), 7.67 (t, 1H), 7.92 (s, 1H), 7.93 (d, 1H), 9.47 (br s, 1H); ^{13}C NMR (100 MHz, $CO(CD_3)_2$, TMS): δ 24.04, 106.90, 111.70, 113.83, 119.97, 120.25, 120.61, 127.59, 134.94, 139.20, 151.76, 157.84, 158.55; MS (EI): $m/z = 338$ (M+).
8. All electrochemical experiments were performed using a CH120A electrochemical workstation. The electrolyte solution was prepared from recrystallised Bu_4NPF_6 using spectroscopic grade dichloromethane (0.1 M) and purged with nitrogen prior to use. A three electrode configuration was used with a Pt working electrode, a Ag wire pseudo reference electrode and a platinum wire as the counter electrode. Decamethylferrocene was used as an internal reference, and the $E_{1/2}$ value of the decamethylferrocene/decamethylferrocenium redox couple was set to 0 mV. Scan rate was 100 mV s^{-1}. $T = 25$°C.
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