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Binding Studies between Tetrathiafulvalene Derivatives and Cyclobis(paraquat-*p*-phenylene)

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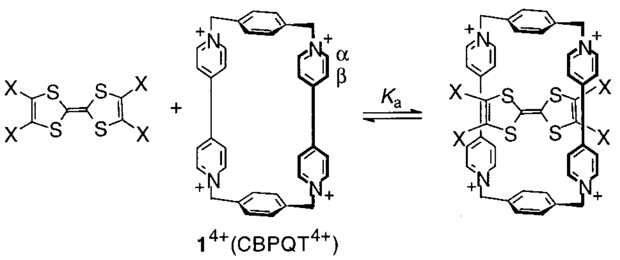
The complexation between a number of different π-electron donating TTF derivatives and the π-electron accepting tetracationic cyclophane cyclobis(paraquat-*p*-phenylene) (CBPQT^{4+}) has been studied by ^{1}H NMR and UV−vis spectroscopy. The results demonstrate that the strength of association between the donors (TTF derivatives) and acceptor (CBPQT^{4+}) is strongly dependent on the π-electron donating properties (measured by the first redox potential $E^1_{1/2}$) of the TTF derivatives. However, the first redox potential ($E^1_{1/2}$) is not the only factor of importance. The extended π-surface of the TTF derivatives also exerts a stabilizing influence upon complexation. The kinetics for the complexation−decomplexation were studied using ^{1}H NMR spectroscopy and are related to the bulkiness of the TTF derivatives. These effects may serve to improve the design of interlocked molecular systems, especially (bistable) molecular switches, in which CBPQT^{4+} and a derivatized TTF unit are incorporated.

Introduction

On account of the ability of the π-electron accepting tetracationic cyclophane,[1] cyclobis(paraquat-*p*-phenylene) (CBPQT^{4+}, **1**$^{4+}$) (Scheme 1), to include π-electron donors within its cavity as a result of stabilizing noncovalent interactions, it has been employed for the construction of a number of mechanically interlocked compounds, such as catenanes and rotaxanes.[2] However, Mirzoian and Kaifer[3] have observed that the best electron donors do not always exert the largest binding affinities with CBPQT^{4+}. Thus, indole forms a stronger complex than catechol, even although indole is a weaker π-electron donor than catechol. The relatively better inclusion of indole is probably the consequence of its larger π-surface.

Scheme 1. Equilibrium for the Formation of 1:1 Complexes between CBPQT^{4+} (1^{4+}) and TTF Derivatives. Note that the K_a Values Quoted in This Article Are for the Tetrakis(hexafluorophosphate) (4PF$_6$$^-$) Salt of 1^{4+}



One of us, and later Bryce, investigated[4] the green 1:1 complex formed between CBPQT^{4+} and the π-electron donor tetrathiafulvalene[5] (TTF, **2**) and found their association to be very strong indeed. A considerable range of catenanes, rotaxanes, and pseudorotaxanes, incorporating different TTF units, and employing CBPQT^{4+} as the encircling component, have been reported.[6] However, the binding affinities between differently substituted TTF

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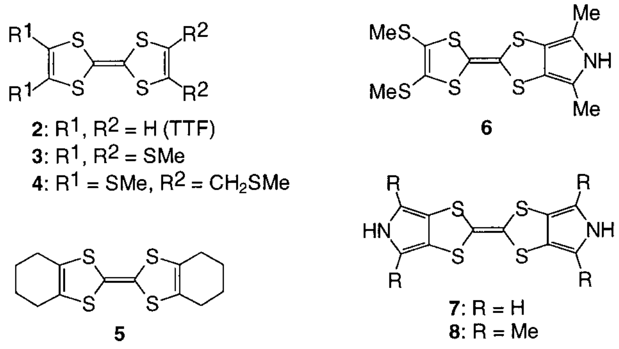

Figure 1. Tetrathiafulvalene (TTF, **2**) and the TTF derivatives **3**−**8** investigated in the present work.

derivatives and CBPQT^{4+} have not been investigated in detail. Therefore, we decided to carry out some binding studies to shed more light on the factors influencing the inclusion of different TTF derivatives inside the cavity of CBPQT^{4+}.

Results and Discussion

The TTFs, which have been investigated in the work reported here, are displayed in Figure 1. All of these TTFs are devoid of polyether substituents capable of forming hydrogen bonds[7] with the α-bipyridinium hydrogen atoms on the tetracationic cyclophane CBPQT^{4+}.

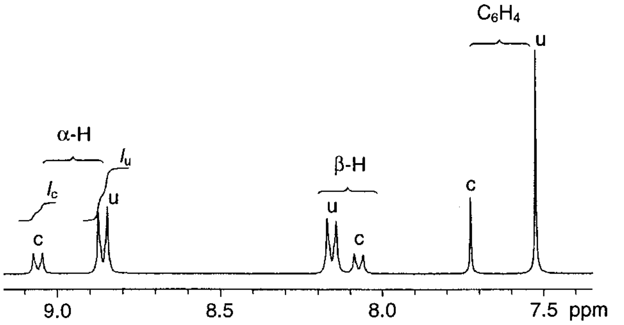

Figure 2. Selected region of the ^{1}H NMR spectrum (250 MHz, CD_3CN, 30 °C) of a 1:2 mixture of CBPQT^{4+} (**1**$^{4+}$) and the TTF derivative **3**. Employing the exact initial concentrations $c(\mathbf{1}^{4+})$ and $c(\mathbf{3})$ the association constant (K_a) can be calculated (eq 1) from the integrals I_c and I_u of complexed (c) and uncomplexed (u) CBPQT^{4+} resonances.

Table 1. ^{1}H NMR Spectroscopic Data (250 MHz, 30 °C) Expressed as Cyclophane CBPQT^{4+} Chemical Shift Changes (Δδ/ppm) upon Complexation of Equivalent Amounts of Different TTFs under Conditions of Slow Exchange between the TTFs and CBPQT^{4+}. Δδ = δ(complexed) − δ(uncomplexed)

compd	solvent	α-H	β-H	C_6H_4	NCH_2
3[a]	CD_3CN	+0.20	−0.08	+0.20	−0.02
3[b]	$(CD_3)_2CO$	+0.34	−0.14	+0.39	0.00
5[c]	$(CD_3)_2CO$	+0.21	−0.18	+0.25	−0.08
8	$(CD_3)_2CO$	+0.18	−0.24	+0.41	−0.05

[a] Values refer to a 1:2 mixture of CBPQT^{4+} and **3**. [b] Values refer to a 1:10 mixture of CBPQT^{4+} and **3**. [c] Values obtained from a 500 MHz spectrum at 0 °C.

Compounds **3**,[8] **4**,[9] **6**,[10] and **8**[11] were observed to be in slow exchange with their CBPQT^{4+} complexes on the ^{1}H NMR time scale (250 MHz, 30 °C), since both complexed and uncomplexed CBPQT^{4+} resonances were present (Figure 2) in the spectra. The cyclophane protons show significant shifts (Table 1) in their resonances upon complexation, which makes it possible to determine association constants (K_a) by employing the ^{1}H NMR single-point method.[12] If I(AB) and I(A) are the integrals of a specific proton in the complexed (AB) and uncomplexed species (A), respectively, and if c(A) and c(B) are the initial molar concentrations of the two uncomplexed components, A and B, then the association constants (K_a) can be calculated[12] from eq 1. By employing this method,

$$K_a = \frac{I(\mathrm{AB})}{I(\mathrm{A})\left(c(\mathrm{B}) - \dfrac{I(\mathrm{AB})}{I(\mathrm{A}) + I(\mathrm{AB})}c(\mathrm{A})\right)} \qquad (1)$$

the K_a values and derived free energies for complexation[13] (−ΔG°) by CBPQT^{4+}of the TTF derivatives **3**, **4**, **6**, and **8** listed in Table 2, together with the K_a value for TTF (**2**) found from ^{1}H NMR titration[4d] (fast exchange, 400 MHz, MeCN, 27 °C), were determined. Complexation is stronger in MeCN than in Me_2CO, a situation that has been observed previously[3] for other donors. Attempts were also made to measure the association constant between CBPQT^{4+} and the very weak donor 2,6(7)-bis(methoxycarbonyl)-3,7(6)-bis(methylthio)TTF, recently employed by some of us as a component of a rotaxane.[6r] The associa-

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[13] The ΔG° values were calculated using the relationship ΔG° = −RT ln K_a, where R is the gas constant and T is the absolute temperature.

Table 2. Comparison of Association Constants (K_a) and Derived Free Energies of Complexation ($-\Delta G°$) between Different TTFs and CBPQT^{4+} Determined by ^{1}H NMR Single-Point Method with the First Redox Potential ($E^1_{1/2}$) for Different TTFs. Temperature: 30 °C unless Otherwise Stated

compd	K_a (M^{-1})^a (Me$_2$CO)	$-\Delta G°$ (kcal mol^{-1}) (Me$_2$CO)	K_a (M^{-1}) (MeCN)	$-\Delta G°$ (kcal mol^{-1}) (MeCN)	$E^1_{1/2}$ (V)^b (MeCN)
8	7900	5.4			+0.33
2			10 000^c	5.5	+0.34
6	1000	4.2			+0.42
4	490	3.7			+0.45
3	40	2.2	180	3.1	+0.51

^{a} Estimated error on K_a: ±10%. ^{b} Half-wave potentials (vs Ag/AgCl) obtained by cyclic voltammetry. ^{c} Found from titration experiments at 27 °C, see ref 4d.

Table 3. Comparison of Association Constants (K_a) and Derived Free Energies of Complexation ($-\Delta G°$) between Different TTFs and CBPQT^{4+} Determined by UV−Vis Spectroscopy with the First Redox Potential ($E^1_{1/2}$) for Different TTFs. Temperature: 22 °C unless Otherwise Stated

compd	K_a (M^{-1})^a (Me$_2$CO)	$-\Delta G°$ (kcal mol^{-1}) (Me$_2$CO)	λ_{max} (nm) (Me$_2$CO)	$E^1_{1/2}$ (V)^b (MeCN)
8	18 000	5.7	870	+0.33
7	12 000	5.5	850	+0.38
2	2600^c	4.6	854	+0.34

^{a} Estimated error on K_a: ±15%. ^{b} Half-wave potentials (vs Ag/AgCl) obtained by cyclic voltammetry. ^{c} At 21 °C, see ref 4c.

tion was, however, much too weak to be measured by either ^{1}H NMR or UV−vis spectroscopies.

In contrast, the TTFs **2**, **5**, and **7**[14] were found to be in fast exchange with their CBPQT^{4+} complexes on the ^{1}H NMR time scale (250 MHz, 30 °C). Bryce and co-workers[4c] have determined the K_a value between TTF (**2**) and CBPQT^{4+} in Me$_2$CO, employing the UV−vis dilution method (Table 3). We have carried out UV−vis dilutions for the complexation of CBPQT^{4+} with the bis(pyrrolo)-TTF derivatives **7** and **8**, by correlating the maximum absorptions of the charge transfer (CT) absorption bands with the concentrations of the components. The absorbances A for the CT bands of 1:1 mixtures of CBPQT^{4+} with both **7** and **8** were measured in situ at several different concentrations (c) in the range 10^{-5}−10^{-4} M. Plotting c/A against $1/A^{1/2}$ afforded a straight line with slope $\alpha = (1/K_a\epsilon l)^{1/2}$ and y intercept $y_0 = 1/\epsilon l$, where ϵ is the molar extinction coefficient for the CT band of the complex and l is the optical path length, according[15] to eq 2. Combining α and y_0 yields $K_a = y_0/\alpha^2$. A representative linear plot of c/A against $1/A^{1/2}$ is shown in Figure 3 for the complexation between CBPQT^{4+} and the bis(pyrrolo)TTF derivative **7**. The association constants (K_a) and derived $-\Delta G°$ values,[13] obtained from the two UV−vis experiments, are recorded in Table 3.

$$\frac{c}{A} = \left(\frac{1}{K_a\epsilon l}\right)^{1/2} \cdot \frac{1}{A^{1/2}} + \frac{1}{\epsilon l} \qquad (2)$$

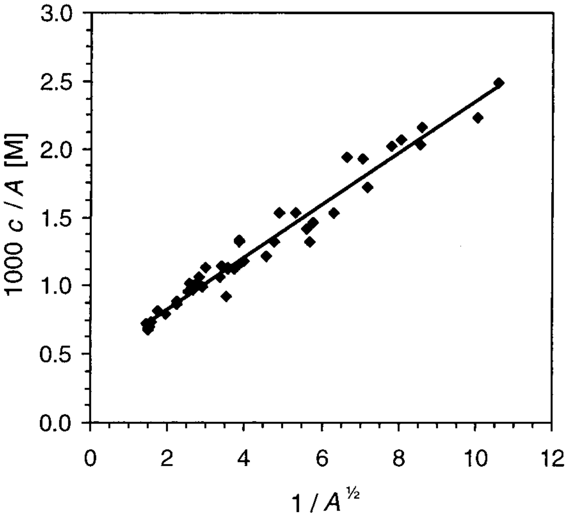

Figure 3. A linear plot of c/A against $1/A^{1/2}$ for a 1:1 mixture of CBPQT^{4+} and the bis(pyrrolo)TTF derivative **7**. The absorbance A was measured at different concentrations c of CBPQT^{4+} (equal to that of **7**) in the range 10^{-5}−10^{-4} M. The data points result from dilutions of eight different stock solutions and have been approximated by the best straight line, giving a correlation coefficient of 0.963.

The K_a values listed in Table 2 reveal a significant trend. As the first redox potential ($E^1_{1/2}$) for the TTF derivatives decreases, the association constant (K_a) increases. Thus, the better is the π-electron donor, the stronger is the complex formed with CBPQT^{4+}. However, the data recorded in Table 3 shows that the first redox potential ($E^1_{1/2}$) is not the only factor of importance. Note that even though the bis(pyrrolo)TTF derivative **7** is a slightly weaker donor than TTF (**2**), it nevertheless exhibits a stronger association with CBPQT^{4+}. It seems that the extended π-surface[16] of the bis(pyrrolo)TTF derivative **7** is exerting a stabilizing influence upon the complex as compared to the parent TTF (**2**). When four electron-donating methyl groups are attached to the pyrrole units, as in the TTF derivative **8**, the association constant increases even further. Previously, we have taken advantage of this strong complexation for preparing catenanes in very high yields by employing macrocyclic derivatives of **8** as the templates for catenation.[6n]

Thus, our thermodynamic data demonstrate clearly that both (i) the π-electron donating properties (measured by the first redox potential $E^1_{1/2}$) and (ii) the area of the π-surface govern the strength of the complexation. It transpires that, for donor−acceptor interactions, the following relationship[17] is obeyed:

$$-\Delta G° = k_1 + T\Delta S° + \frac{k_2\beta^2}{E^1_{\text{donor}} - E^1_{\text{acc}}} \qquad (3)$$

where k_1 and k_2 are constants and β is the overlap integral between donor and acceptor, while E^1_{donor} and E^1_{acc} are the first redox potentials of the donor (TTF

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(15) Equation 2 was determined as reported in the Supporting Information. For further information, see: Colquhoun, H. M.; Goodings, E. P.; Maud, J. M.; Stoddart, J. F.; Wolstenholme, J. B.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 2* **1985**, 607−624.

(16) The character of the highest occupied molecular orbital (HOMO) of the bis(pyrrolo)TTF **7** has recently been calculated and shows that approximately 21% of the HOMO density is located on the outher two pyrrole rings, see ref 14b.

(17) *Donor−Acceptor Bond*; Gur'yanova, E. N., Gol'dshtein, I. P., Romm, I. P., Eds.; (translated from Russian by R. Kondor, translation edited by D. Slutzkin) Koterpress Enterprises: Jerusalem, Israel, 1975.

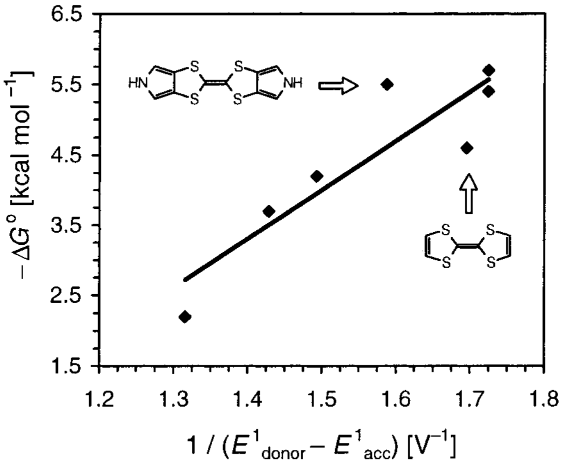

Figure 4. Plot of $-\Delta G°$ in Me_2CO vs the reciprocal difference in redox potentials between π-electron donor (TTF derivative) and π-electron acceptor ($CBPQT^{4+}$) units. The seven data points have been approximated by the best straight line.

derivative) and acceptor ($CBPQT^{4+}$) entities. Figure 4 shows a plot of $-\Delta G°$ in Me_2CO vs the reciprocal difference $1/(E^1_{\text{donor}} - E^1_{\text{acc}})$ in redox potentials for the TTFs **2**−**4** and **6**−**8**, using for the cyclic $CBPQT^{4+}$ acceptor[18] $E^1_{\text{acc}} = -0.25$ V (vs Ag/AgCl in MeCN). Deviations from a straight line originate mainly from different overlap integrals β. Note that the overlap is smaller for unsubstituted TTF (**2**), carrying neither sulfur-containing nor pyrrolo substituents.

Although the tetrakis(thiomethyl)-substituted TTF derivative **3** exhibits the weakest association of all with $CBPQT^{4+}$, the K_a value is still relatively high—and a number of catenanes and rotaxanes have been prepared[4b,6a−g,j,k] from macrocyclic polyethers containing units of **3**. It is also important to note that recent calculations[7] have shown that the ethyleneoxy groups are of paramount importance in assisting the complexation process by virtue of their entering into [C−H···O] interactions with some of the α-CH hydrogen atoms in the bipyridinum units of $CBPQT^{4+}$. Indeed, the association constant for a polyether-linked TTF derivative has been determined[6m] to be approximately 10 000 M^{-1}. Also, complexation studies show[19] that 1,4-bis(2-(2-hydroxyethoxy)ethoxy)benzene associates with $CBPQT^{4+}$ to form a stronger complex ($K_a = 2200$ M^{-1}, MeCN, 25 °C) than does ($K_a = 18$ M^{-1}, MeCN, 25 °C) 1,4-dimethoxybenzene.

Whether a TTF derivative and the cyclophane $CBPQT^{4+}$ are in fast exchange or not with their complex on the ^1H NMR time scale is influenced largely by the bulkiness of the TTF derivative. Hence, substituting the TTF core with two $(CH_2)_4$ groups, as in the case of **5**, does not change the equilibrium from being fast on the 250 MHz time scale (at 30 °C). However, four bulky SMe groups, as in the case of **3**—or two SMe and two CH_2-SMe groups, as in the case of **4**—change the kinetics from fast into slow exchange. The bis(pyrrolo)TTF derivative **7** undergoes fast exchange with its $CBPQT^{4+}$ complex, but attachment of four Me substituents, as in the case of **8**, changes the kinetics into slow exchange on the 250 MHz time scale (30 °C). Thus, the exchange rate is a result of a fine balance between electronic and steric factors. Probing a sample of $CBPQT^{4+}$ and **5** at a smaller time scale (500 MHz, 25 °C) shifts the kinetics into an intermediate exchange region (Figure 5a). Upon cooling this sample down to 0 °C, a slow exchange process is observed (Figure 5b).

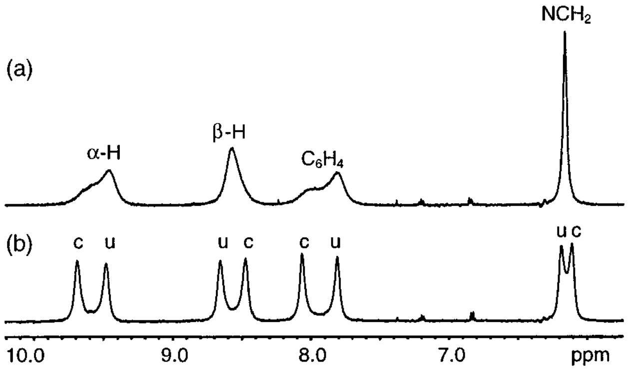

Figure 5. Partial (cyclophane region) ^1H NMR spectra (500 MHz) of the complex between $CBPQT^{4+}$ and the TTF derivative **5** in $(CD_3)_2CO$ at (a) 25 °C and (b) 0 °C. Notation: c = complexed $CBPQT^{4+}$; u = uncomplexed $CBPQT^{4+}$.

Conclusion

In summary, the complexation properties of different π-electron donating TTF derivatives by the π-electron accepting tetracationic cyclophane, $CBPQT^{4+}$, have been investigated by ^1H NMR and UV−vis spectroscopy. Three major conclusions can be drawn: (i) The stronger the donor, the higher the association constant (K_a).[20] (ii) Extension of the π-system of the TTF derivative increases the extent of the association. (iii) The kinetics for the complexation−decomplexation are related to the bulkiness of the TTF derivative. These findings are of fundamental importance in designing (bistable) molecular switches[6q,21,22] based on catenanes, rotaxanes, and pseudorotaxanes in which one of the π-electron donating sites in one component is a derivatized TTF unit and the other recognition component is cyclobis(paraquat-*p*-phenylene).

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Experimental Section

The cyclic acceptor cyclobis(paraquat-*p*-phenylene) ($\mathbf{1}^{4+}$), which was used as its tetrakis(hexafluorophosphate)($4PF_6^-$) salt, was synthesized according to the procedure reported in the literature.[1c] TTF (**2**) and 4,4′,5,5′,6,6′,7,7′-octahydrodibenzoTTF (**5**) were purchased from Aldrich and used as received. The TTF derivatives **3**,[8] **4**,[9] **6**,[10] **7**,[14] and **8**[11] were prepared according to published procedures. ^{1}H NMR spectra were recorded on a Bruker AC-250 or a Varian 500 spectrometer at 250 and 500 MHz, respectively. UV−vis spectra were recorded at 22 °C in Me_2CO on a Shimadzu UV-160 instrument.

Determination of Association Constants (K_a) Using the ^{1}H NMR Single-Point Method. Mixing $\mathbf{1}\cdot 4PF_6$ and the TTF derivatives in a ratio from 1:1 to 1:10 in either CD_3CN (TTF derivative **3**) or $(CD_3)_2CO$ (TTF derivatives **3**, **4**, **6**, and **8**) at concentrations of 10^{-4}−10^{-3} M produced green-colored solutions. The K_a values were determined from the ratio of integrals for complexed and uncomplexed compounds according to eq 1 (see Supporting Information for further details). For the complex between $\mathbf{1}\cdot 4PF_6$ and **3**, a 2-fold excess of **3** relative to $\mathbf{1}\cdot 4PF_6$ in CD_3CN and a 10-fold excess of **3** relative to $\mathbf{1}\cdot 4PF_6$ in $(CD_3)_2CO$ was necessary in order to observe the complexed signals of $\mathbf{1}^{4+}$. Each K_a value recorded in Table 2 was obtained from the average of at least three independent measurements.

Determination of Association Constants (K_a) Using the UV−Vis Dilution Method. Mixing $\mathbf{1}\cdot 4PF_6$ and either the bis(pyrrolo)TTF derivatives **7** or **8** in equimolar proportions in Me_2CO at 22 °C produced a green-colored solution as a result of the appearance of a charge-transfer absorption band, centered on $\lambda_{max} = 850$ or 870 nm for **7** and **8**, respectively. The absorbance A (at λ_{max}) was measured at several different concentrations (c) in the range of 10^{-5}−10^{-4} M. Measurements were carried out from dilutions of either 8 or 10 different stock solutions, which resulted in 44 or 57 data points [c/A, $1/A^{1/2}$] for **7** and **8**, respectively. In each experiment the linear relationship (see Figure 3) between c/A and $1/A^{1/2}$ was demonstrated by calculation of the correlation coefficients. Values of 0.963 and 0.929 were obtained for **7** and **8**, respectively. K_a values were obtained from the relationship $K_a = y_0/\alpha^2$, where α and y_0 are the slope and y intercept of the line, respectively (see Supporting Information for further details).

Electrochemical Measurements. Electrochemical experiments were carried out at room temperature in a nitrogen-purged MeCN solution with an Autolab/PGSTAT 10 instrument interfaced to a personal computer, using cyclic voltammetry (CV) technique. Working and counter electrodes were made of Pt, and the reference electrode was Ag/AgCl. The concentration of the examined compounds was 10^{-3} M, and 0.10 M [n-Bu_4N][PF_6] was added as supporting electrolyte. Cyclic voltammograms were obtained with a sweep rate of 100 mV s^{-1}. All TTF derivatives exhibited two pairs of reversible redox waves corresponding to two one-electron processes. The first half-wave potentials ($E^1_{1/2}$), reported in Tables 2 and 3, were obtained from an average of the cathodic and anodic cyclic voltammetric peaks.

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Supporting Information Available: Derivation of eq 2, tables listing the absorbance for the UV−vis experiments, linear plots of c/A against $1/A^{1/2}$, and an example of calculation of K_a using the ^{1}H NMR single-point method. This material is available free of charge via the Internet at http//pubs.acs.org.

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