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Electrochemical Recognition of Cations by Bis(pyrrolo)tetrathiafulvalene Macrocycles

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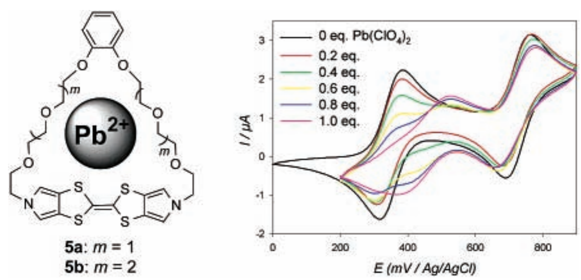
ABSTRACT



Tetrathiafulvalene redox-responsive ligands devoid of cis/trans isomerism containing the electroactive bis(pyrrolo[3,4-*d*])tetrathiafulvalene moiety and polyether subunits have been synthesized. One ligand exhibits high binding affinities for Pb^{2+} and Ba^{2+} cations as shown by independent methods (^{1}H NMR, UV–vis spectroscopy, and cyclic voltammetry). The ability of this receptor to electrochemically recognize Pb^{2+} and Ba^{2+} is shown by cyclic voltammetry.

Host−guest chemistry plays a central role in supramolecular chemistry[1] and the development of macrocyclic ligands for which complexation of a neutral or ionic guest induces a change in the optical[2] or redox[3] properties of the systems continues to provide a challenge for supramolecular chemists. Redox-responsive ligands can be built from the covalent association of a redox-active unit to a host unit, allowing the complexing properties toward an appropriate guest to be controlled by the redox state of the electroactive unit.[3] The redox-active tetrathiafulvalene[4] (TTF, **1**) (Figure 1) unit

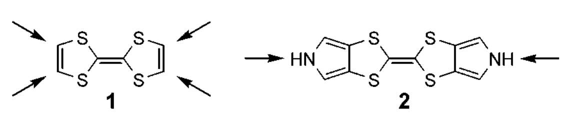


Figure 1. Structure of tetrathiafulvalene (**1**) and bis(pyrrolo[3,4-*d*])tetrathiafulvalene (**2**).

is associated with the preparation of molecular organic metals. Nevertheless, recent development[4] in synthetic TTF chemistry has revolutionized the possibilities for incorporation of TTF into macrocyclic, molecular, and supramolecular structures and has transformed complicated systems such as

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TTF-cyclophanes,[4d,e] TTF-catenanes,[4d,e] and TTF-rotaxanes/pseudorotaxanes[4d,e,5] from chemical curiosities into a vibrant area of modern-day research. In the context of redox-responsive ligands, the TTF unit appears as an ideal redox-active system in view of its unique π-electron-donating properties.[6] Its oxidation to the radical cation ($TTF^{+\bullet}$) and dication (TTF^{2+}) occurs sequentially and reversibly at low potentials, and such a reversibility of its redox processes can allow the electrochemical control of trapping (neutral TTF) or releasing (cationic TTF) of a given metallic cation, simply by changing the redox state of the TTF core. Incorporation of the TTF unit into macrocycles containing a crown ether recognition motif has been well documented[4c−e,6] in recent years and has allowed the electrochemical recognition of various metal cations. Until now, and essentially for synthetic reasons, the TTF unit has mainly been introduced into macrocyclic systems as a tetrathioTTF moiety.[6] Since the TTF core presents four identical potential attachment sites (Figure 1), incorporation of the tetrathioTTF moiety into macrocyclic systems often results in the isolation of cis/trans isomeric[7] mixtures, as in the case of the TTF-crown[6l] **3** (Figure 2). This inherent cis/trans isomerism may alter the complexing ability of the ligand. Indeed, liquid solution ionization mass spectrometry (LSIMS) and ^{1}H NMR spectroscopy showed that only the cis-isomer of **3**, is able to complex[6l] Ba^{2+}. Furthermore, a cis/trans isomerization has been shown to take place in solution for related compounds.[6l,8] Recently, the synthesis of bis(pyrrolo[3,4-*d*])tetrathiafulvalene (**2**) (Figure 1) has been reported.[9] This TTF derivative can easily be functionalized by *N*-alkylation of its two pyrrole units, thereby allowing the preparation of macrocyclic systems devoid of cis/trans isomerism.[10]

In this Letter, we report the synthesis of the first examples of macrocycles **4a**,**b** and **5a**,**b** (Figure 2) incorporating the

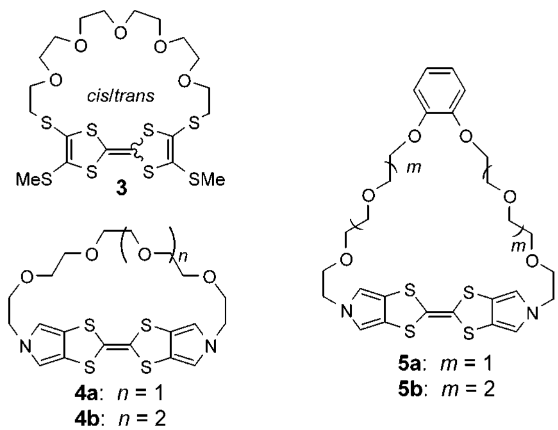
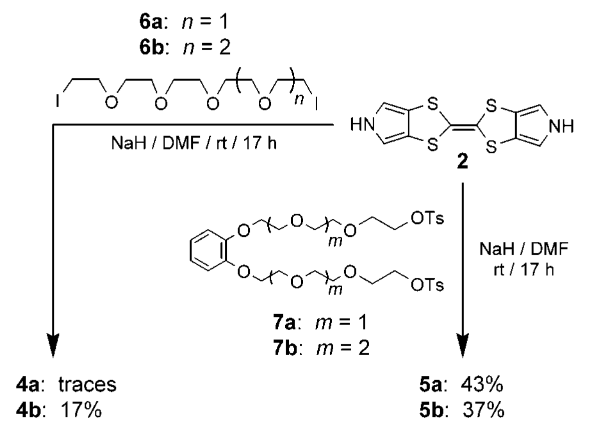


Figure 2. Polyether-fused TTF and bis(pyrrolo)TTF.

bis(pyrrolo)TTF moiety **2** and demonstrate that one of them (i.e., **5b**) acts as a redox responsive ligand toward Ba^{2+} and Pb^{2+}.

The macrocycles **4a**,**b** and **5a**,**b** were synthesized as outlined in Scheme 1. Bis(pyrrolo)TTF **2** was synthesized

Scheme 1. Synthesis of the Macrocycles **4a,b** and **5a,b**



according to the literature procedure,[9] whereupon *N*,*N′*-functionalization of **2** was carried out using high-dilution conditions. Simultaneous slow addition (perfusor pump, 3 mL h^{-1}) of **2** and an appropriate ω-diiodo poly(ethylene glycol) derivative[11] **6a**,**b** or a cathecol derivative[12] **7a**,**b** onto a slurry of NaH in DMF produced compounds **4a**,**b** and **5a**,**b**. This kind of bis substitution ensures a close proximity between the coordinating unit and the central electroactive

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TTF framework, which is necessary in order to optimize the response of the electroactive part upon complexation of a metal cation. It transpires from Scheme 1 that the yield of isolated [1 + 1] macrocyclization product is much lower for **4b** than in the case of compound **3** (50% isolated yield)[6l] although the linker used for the macrocyclization is the same. This observation is presumably a direct consequence of the larger size (ca. +30%) of the rigid part of the bis(pyrrolo)-TTF moiety as compared to the tetrathioTTF one, and therefore the use of larger linkers is needed when bis-(pyrrolo)TTF **2** is used as the electroactive unit. This is consistent with the fact that only traces of **4a**, involving a shorter polyethylene linker, could be isolated, and that yields are much better for the larger cathecol derivatives **5a**,**b**.

Geometry optimizations at the semiempirical level (PM3) have also been carried out. The calculations shows (Figure 3) that the bending angles, **4a** (24°), **4b** (15°), **5a** (11°), and

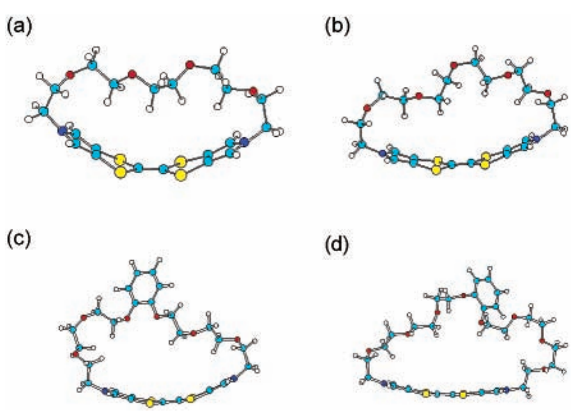


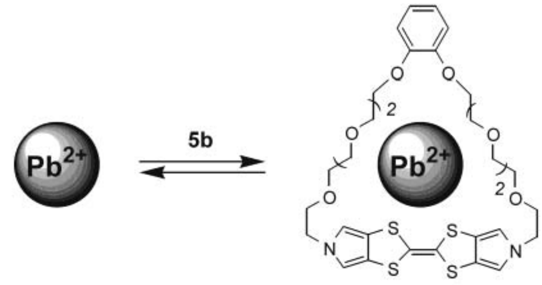
Figure 3. Geometry optimization (PM3, Hyperchem) of the macrocyclic ligands (a) **4a**, (b) **4b**, (c) **5a**, and (d) **5b**.

5b (6°), in the central TTF part are regularly smaller when the number of oxaethylene fragments increases. The flattening of the electroactive unit, as observed in compound **5a**,**b**, constitutes a crucial prerequisite for the recognition properties of the macrocyclic ligand, since the integrity of the electrochemical behavior, and in particular electrochemical reversibility, of the redox systems is greatly affected by this structural parameter.[6l]

The binding properties of the macrocyclic receptors **4a**,**b** and **5a**,**b** toward cations were evaluated using different techniques including ^{1}H NMR and UV−vis spectroscopy, LSIMS, and cyclic voltammetry (CV). The most spectacular results were obtained from the larger ligand **5b**, which shows remarkable sensing properties in the cases of Ba^{2+} and Pb^{2+}.

A comparison of the ^{1}H NMR spectra (CD_3CN/$CDCl_3$ (1:1), 298 K) of the free macrocycle **5b** and the macrocycle **5b** in the presence of $Pb(ClO_4)_2$ reveals significant chemical shift differences for the resonances associated with the oxamethylene protons of the linker and the aromatic protons on the cathecol unit, indicating that Pb^{2+} is complexed (Scheme 2) within the macrocyclic receptor **5b**.

Scheme 2. Complexation of Pb^{2+} by the Macrocyclic Receptor **5b**



5b·Pb^{2+}

^{1}H NMR titration experiments[6l] were carried out to determine the binding constant ($K°$) for the complex of Pb^{2+} and the macrocyclic receptor **5b** in a 1:1 mixture of CD_3CN and $CDCl_3$ at 298 K. Addition of increasing amounts of Pb-$(ClO_4)_2$ to a solution of **5b** induced complexation which was followed (Figure 4) by observing the changes in the chemical

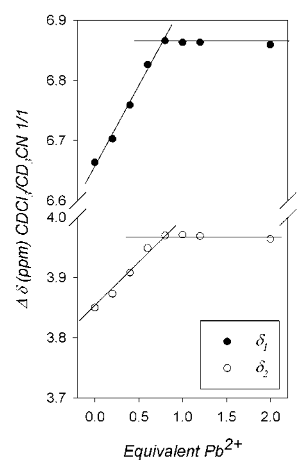


Figure 4. ^{1}H NMR titration curves of the perturbation of CH_2O (○) and aromatic protons (●) of **5b** (7.6×10^{-3} mol L^{-1}) upon addition of increasing amounts of Pb^{2+}.

shifts. Addition of an excess Pb^{2+} (>1.0 equiv) did not cause any further changes in the ^{1}H NMR spectrum of **5b**, which confirms a 1/1 stoichiometry for the complexation of Pb^{2+} by **5b**. The binding constant was obtained using the curve fitting program[13] EQNMR and gave an average log $K°$ value of 6.2 for the **5b**·Pb^{2+} complex (from different chemical shifts).

Cyclic voltammetry (CV) is a powerful tool to evaluate the recognition properties of a redox-responsive ligand. The progressive addition of Pb^{2+} to solution of **5b** (CH_3CN/CH_2-Cl_2 (1/1)) caused significant modifications in the CVs (Figure 5) and the emergence of a new redox wave. Thus, for

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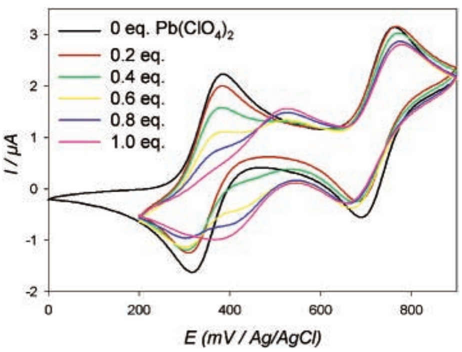

Figure 5. Cyclic voltammograms of **5b** recorded in a mixture of CH_2Cl_2 and CH_3CN (10^{-3} mol L^{-1}) and Bu_4NPF_6 (10^{-1} mol L^{-1}) as the supporting electrolyte in the presence of increasing amounts of Pb^{2+}.

addition of molar equivalents between 0 and 1, the first redox process of the bis(pyrrolo)TTF unit is divided into two different redox systems as a result of the coexistence of the free ligand **5b** (anodic peak potential: $E_1^{ox} = 0.38$ V) and the complex **5b**·Pb^{2+} ($E_1^{ox} = 0.52$ V). Therefore, $\Delta E_1^{ox} =$ 140 mV, which is the highest value observed so far for ligands based on TTF and can be attributed to the remarkable binding properties of **5b** for Pb^{2+}. Furthermore, it is noteworthy that the second oxidation potential remains unaltered after addition of Pb^{2+}, which gives an indirect proof of the release of the metal cation, when the bis(pyrrolo)TTF unit is oxidized to the dicationic state. Binding constants of the complex **5b**·Pb^{2+} have been evaluated on the basis of a square scheme,[6l] by simulation of the cyclic voltammograms using a fitting program (DIGISIM 3.0 from BAS Inc.).[14] As expected, the binding properties of **5b** are directly correlated to the oxidation state of the bis(pyrrolo)TTF core. First, though lower than evaluated by ^{1}H NMR titration, a very strong affinity is found for the neutral state (log $K° = 4.7$); second, a decrease of the complexation ability is observed for the radical-cation state (log $K^{+\bullet} = 2.9$), and finally, the total expulsion of Pb^{2+} from **5b** at the dicationic state ($K^{2+} \approx 0$).

Concurrently, **5b** also shows good binding properties toward Ba^{2+}. ^{1}H NMR titration of **5b** with $Ba(ClO_4)_2$ carried out in a 1:1 mixture of $CDCl_3$ and CD_3CN at 298 K indicates a 1/1 stoichiometry of the complex **5b**·Ba^{2+} and analysis of the data gave a log $K°$ value of 5.3 for the complex **5b**·Ba^{2+}. In the case of **5b**·Ba^{2+}, the positive displacement of the first oxidation potential (i.e., ΔE_1^{ox}) in the CVs reaches a value of 90 mV. Simulated binding constants evaluated in a 1:1 mixture of $CDCl_3$ and CD_3CN for the different redox states of the bis(pyrrolo)TTF gave the following values: log $K° = 4.8$ for neutral **5b**, log $K^{+\bullet} = 3.4$ for **5b**$^{+\bullet}$, and $K^{2+} \approx$ 0 for **5b**$^{2+}$. Finally, the complexation of Ba^{2+} by **5b** was investigated by UV−vis spectroscopy. Addition of $Ba(ClO_4)_2$ to a solution of **5b** (CH_3CN/CH_2Cl_2 (1/1), 298 K) induces significant modifications in the UV−vis spectra (Figure 6).

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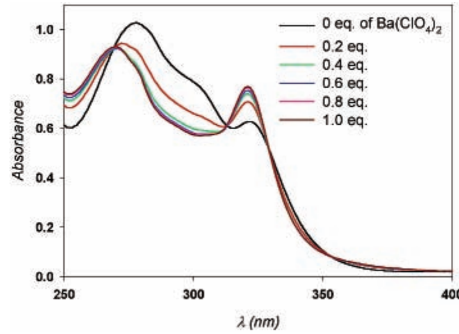

Figure 6. Absorption spectra of **5b** recorded in a 1:1 mixture CH_2Cl_2 and CH_3CN (2.6×10^{-4} mol L^{-1}) in the presence of increasing amounts of Ba^{2+}.

Four isobestic points (269, 313, 329, and 352 nm) are observed in accordance with the existence of only two species, the free ligand **5b** and the complex **5b**·Ba^{2+}. The binding constant for the complexation of Ba^{2+} by **5b** was determined by the Benesi−Hildebrand method.[15] A log K value of 4.9 ($r = 0.998$) was obtained, which is in good agreement with the value obtained by ^{1}H NMR titration, and confirms the good recognition properties of **5b** toward Ba^{2+}.

In summary, TTF-based macrocyclic ligands devoid of cis/trans isomerism have been synthesized. The bis(pyrrolo)-TTF-crown **5b** exhibits remarkable high binding affinities, in its neutral state, toward Pb^{2+} and Ba^{2+}. Binding constants in the range of 10^5 to 10^6 were obtained from titration studies, which correspond to the highest binding constants reported so far for a TTF-based ligand. Furthermore, it has been demonstrated that the binding properties of **5b** can be modified simply by changing the redox state of the bis(pyrrolo)TTF moiety, thereby allowing a controlled uptake (neutral **5b**) and release (**5b**$^{2+}$) of the cation from the ligands cavity. A fundamental understanding of such simple redox responsive ligands can aid the design of more complicated systems that may find applications as new sensors or as novel drug delivery systems.

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Supporting Information Available: Experimental procedure and characterization data for compounds **4**, **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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