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Selective Redox-Active Molecular Receptors for K^+ and Ag^+

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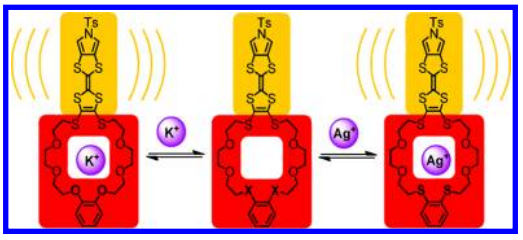
ABSTRACT



Two new tetrathiafulvalene based receptors in which the favorable redox properties of the tetrathiafulvalene unit are coupled to either a benzo-crown (X = O) or a dithiabenzo-crown (X = S) ether binding site were designed and synthesized as receptors for K^+ and Ag^+. The receptors display a good (K^+, X = O) to strong (Ag^+, X = S) affinity toward the cation and a high discrimination against other metal cations.

The advent of supramolecular chemistry[1] has aroused the interest of chemists of many different persuasions in the development of molecular receptors capable of recognizing specific chemical substrates. Redox-active receptors[2] are of particular interest because their affinity toward different substrates are reflected by the redox properties of the receptor allowing supramolecular systems capable of performing controlled uptake and release of substrates to be constructed. Redox-active molecular receptors are typically designed to allow the detection of substrates by binding-induced changes in the redox properties and are generally being built by the covalent association of an appropriate binding site and a redox-active unit. In the context of redox-active receptors, tetrathiafulvalene[3] (TTF) constitutes a unique building block on account of the fact that it can exist in three stable redox states (i.e., as neutral TTF, as the radical cation $TTF^{\bullet+}$, and the dicationic TTF^{2+}) and TTF and its derivatives have been used as the redox-active unit in a number of anion[4] and cation[5] responsive receptors. A majority of the cation responsive receptors involve a binding site made of a crown-ether cavity or a coordinating acyclic ether moiety.[6] Although a huge amount of work has been devoted to create TTF

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based receptors with high sensitivity toward cations, selectivity has received much less attention.

Here, we describe the synthesis and characterization of two unique TTF based receptors in which the favorable redox properties of the monopyrrolo-TTF[7] (MPTTF) unit are coupled to either a benzo-crown (**1**) or a dithiabenzo-crown (**2**) ether binding site. Subsequently, binding studies between the receptors **1** and **2** and a variety of cations are described and it is demonstrated that the oxygen/sulfur atoms attached to the benzo moiety in the redox-active receptors control the selectivity toward K^+ and Ag^+.

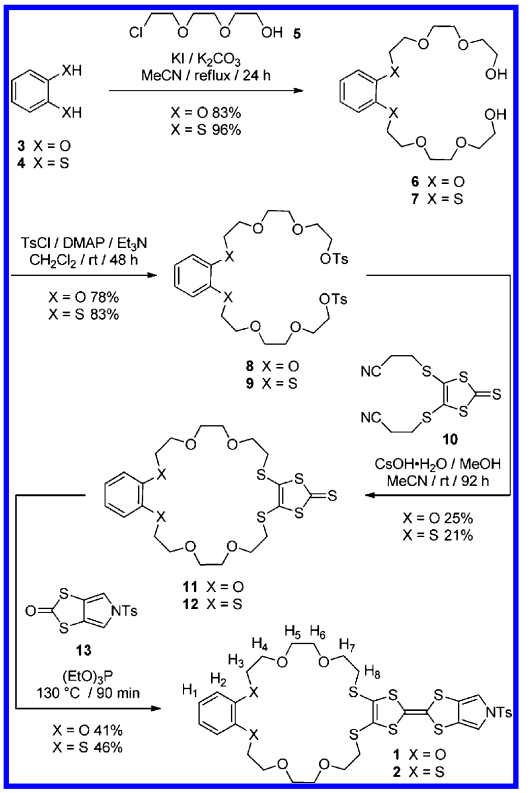
The MPTTF crown ethers **1** and **2** were synthesized as illustrated in Scheme 1.[8] Cathecol **3** and dithiole benzene **4** were alkylated with the glycol derivative **5** in MeCN in the presence of K_2CO_3 and KI to afford compounds **6**/**7** as pale yellow oils in high yields (83/96%). The two alcohol groups in **6** and **7** were tosylated using TsCl in CH_2Cl_2 in the presence of 4-dimethylaminopyridine (DMAP) and Et_3N affording **8** or **9** in 78 or 83% yield, respectively. Subsequent treatment of **8** or **9** with 4,5-bis(2-cyanoethylthio)-1,3-dithiole-2-thione[9] (**10**) under high-dilution conditions using CsOH as the base gave the macrocyclic crown ether **11** or **12** in approximately 25% yield. Finally, cross-couplings of **11** and **12** with 5-tosyl-(1,3)-dithiolo[4,5-*c*]pyrrole-2-one[10] (**13**) in neat $(EtO)_3P$ gave the MPTTF crown ethers **1** and **2** in 41 and 46% yields, respectively.

The MPTTF receptor molecules **1** and **2** were isolated as analytically pure yellow solids and high-resolution electrospray ionization mass spectrometry (HiRes-ESI-MS) of **1** and **2** produced peaks with the exact masses of m/z = 799.0520 and 853.9961, respectively, corresponding to the expected molecular ions $M^{\bullet+}$ (calcd $M^{\bullet+}$ = 799.0559 and 853.9999, respectively).

A comparison of the ^{1}H NMR spectra of **1** and **2** recorded in $CDCl_3$ at 298 K reveals (Figures S1 and S2) significant differences. In **1**, the resonances associated with the aromatic H_1 and H_2 protons (Scheme 1) were observed as a 4 H multiplet at δ = 6.89 ppm, whereas the H_1 and H_2 protons in **2** were observed as two 2 H multiplets resonating at δ = 7.14 and 7.33 ppm, respectively, an observation that can be accounted for by the different substitutions of the benzene ring (i.e., oxygen vs sulfur). In compound **2**, two triplets each integrating to 4 H were observed in the aliphatic region between 2.75 and 3.25 ppm, a feature that was assigned to the two chemically different SCH_2 groups present in **2**, whereas only one 4 H triplet was observed in the 2.75−3.25 ppm region for **1**. The remaining aromatic and aliphatic protons in **1** and **2** all appeared at the expected chemical-shift values (see Supporting Information).

To increase the solubility and dissociation of KPF_6 and $AgPF_6$, the solution-state binding studies involving the

Scheme 1. Synthesis of the Receptor Molecules **1** and **2**



receptors **1** and **2** and different cations were carried out in a 1:1 mixture of CH_2Cl_2/MeCN (UV−vis spectroscopy and cyclic voltammetry) or in a 1:1 mixture of $CDCl_3/CD_3CN$ (NMR spectroscopy).

Initial evidence for the interactions between the receptors **1** and **2** and K^+/Ag^+ came from UV−vis absorption spectroscopy. When KPF_6 was added to a solution (CH_2Cl_2/MeCN (1:1), 298 K) of the receptor **1** significant spectral changes were observed. Figure 1a shows the spectral changes of **1** upon addition of 0−7 equiv of KPF_6. As the concentration of KPF_6 was increased, the intensity of the absorption band at 350 nm decreases, while the intensity at 410 nm increases leading to the formation of two isosbestic points at 320 and 375 nm, respectively. This observation is consistent with the formation of only two absorption species, the free receptor **1** and the **1**•K^+ complex. The resulting binding profile (Figure 1a, insert) was subjected to a standard nonlinear (1:1 host/guest) curve fitting analysis[11] from which a binding constant (K_a) of 2000 M^{-1} (±20%) for the **1**•K^+ complex was obtained. Similar titration experiments were carried out with Ag^+, Pb^{2+}, Hg^{2+}, Cd^{2+}, Pd^{2+}, Zn^{2+}, Na^+, and Li^+. However, no perceptible changes in the UV−vis absorption spectra were observed indicating that the receptor **1** is highly selective toward K^+.

UV−vis titration experiments carried out between the receptor **2** and K^+, Ag^+, Pb^{2+}, Hg^{2+}, Cd^{2+}, Pd^{2+}, Zn^{2+}, Na^+, and Li^+ reveal that only in the case of Ag^+ significant

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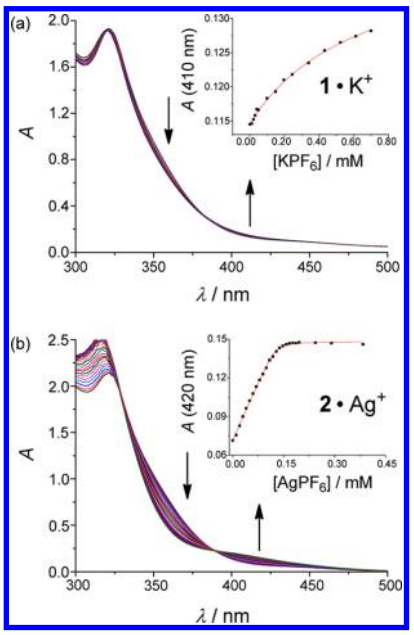

Figure 1. (a) UV−vis spectra recorded in CH_2Cl_2/MeCN (1:1) at 298 K of a 0.1 mM solution of **1** upon titration with K^+. The insert shows the binding profile obtained using the 410 nm band as a probe and its nonlinear curve fit to a 1:1 model. (b) UV−vis spectra recorded in CH_2Cl_2/MeCN (1:1) at 298 K of a 0.1 mM solution of **2** upon titration with Ag^+. The insert shows the binding profile obtained using the 420 nm band as a probe and its nonlinear curve fit to a 1:1 model.

changes were observed in the UV−vis absorption spectra. Titration (Figure 1b) of $AgPF_6$ into a solution (CH_2Cl_2/MeCN (1:1), 298 K) of the receptor **2** shows that the intensity of the absorption band at 370 nm decreases while the intensity at 420 nm increases with the concomitant formation of two isosbestic points at 328 and 385 nm, respectively. This feature indicates the presence of only two absorption species, the free receptor **2** and the complex **2**•Ag^+. A nonlinear curve fitting analysis[11] of the resulting binding profile (Figure 1b, insert) afforded a K_a value of 700 000 M^{-1} (±20%) for the **2**•Ag^+ complex indicating that the receptor **2** is both highly sensitive[12] and selective toward Ag^+.

A comparison (Figure 2) of the ^{1}H NMR spectra (400 MHz, 298 K) recorded in a 1:1 mixture of $CDCl_3$ and CD_3CN of the free receptor **2** and the receptor **2** in the presence of $AgPF_6$ reveals significant chemical-shift differences for several of the resonances associated with the protons in the receptor **2**, which indicates that the Ag^+ ion is complexed to **2**. In particular, the resonances associated with the aromatic protons (Scheme 1) are downfield shifted from δ = 7.25 ppm to δ = 7.62 ppm ($\Delta\delta$ = +0.37 ppm) and from δ = 7.42 ppm to δ = 7.95 ppm ($\Delta\delta$ = +0.53 ppm) for H_2 and H_1, respectively, whereas the aliphatic H_4 and H_7 protons (Scheme 1) are upfield shifted from δ = 3.75 ppm to δ = 3.27 ppm ($\Delta\delta$ = −0.48 ppm) and δ = 3.60 ($\Delta\delta$ = −0.15 ppm) indicating that these protons are highly affected by the complexation of Ag^+ inside the cavity of the dithiabenzo-crown ether moiety. Addition of more than 1 equiv of Ag^+ did not cause any significant changes in the ^{1}H NMR spectra of **2**, thus confirming that **2** forms a 1:1 complex with Ag^+. As a consequence of the strong binding (vide supra) between the receptor **2** and Ag^+ and the fact that the ^{1}H NMR titration experiments were carried out with the concentration of **2** 20 times higher than in the case of the corresponding UV−vis titration experiments, it was not possible to obtain a reliable K_a value for the binding between **2** and Ag^+ using ^{1}H NMR spectroscopy, because the binding profile tended toward linearity with increasing Ag^+ concentration, which made the nonlinear curve fitting procedure unreliable[13] for estimating the K_a value.

Similar ^{1}H NMR spectroscopic titration experiments were conducted with solutions containing K^+, Pb^{2+}, Hg^{2+}, Cd^{2+}, Pd^{2+}, Zn^{2+}, Na^+, and Li^+. However, no perceptible changes in the ^{1}H NMR spectra were observed supporting the notion that the **2** is highly selective toward Ag^+.

The binding between receptor **1** and K^+, Ag^+, Pb^{2+}, Hg^{2+}, Cd^{2+}, Pd^{2+}, Zn^{2+}, Na^+, and Li^+ were also studied using ^{1}H NMR spectroscopy. As observed in the UV−vis titration experiments (vide supra), only the addition of KPF_6 to a solution ($CDCl_3$/CD_3CN (1:1), 298 K) of the receptor **1** produced observable changes in the ^{1}H NMR spectra (Figure S20). However, the observed chemical-shift differences for the formation of the **1**•K^+ complex were smaller and required a higher concentration of the cation as

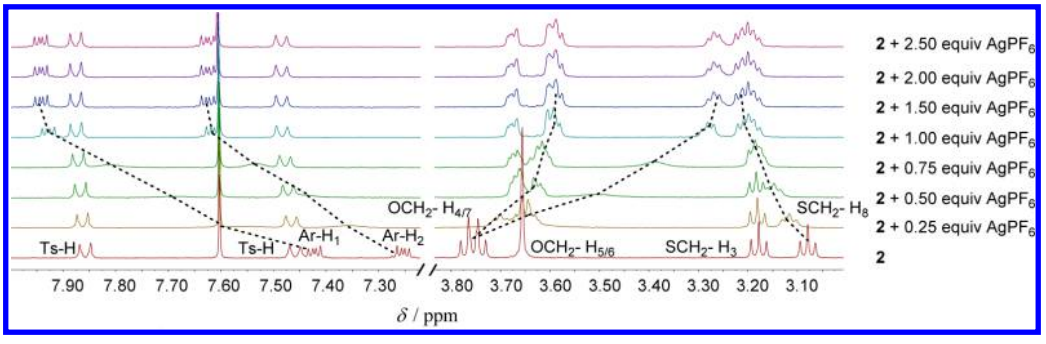

Figure 2. Partial ^{1}H NMR spectra (400 MHz, 298 K) recorded in a 1:1 mixture of $CDCl_3$/CD_3CN of the receptor **2** (2 mM) upon titration with Ag^+.

compared to the formation of the **2**•Ag^+ complex indicating that the **1**•K^+ complex is weaker than the **2**•Ag^+ complex. UV−vis and ^{1}H NMR spectroscopic studies revealed that **1** and **2** are able to complex cations in solution. However, these receptors were also designed to allow the binding events to be followed via cation-induced changes in the electrochemical properties of the MPTTF units. Cyclic voltammetry (CV) was used to probe the changes in the redox potentials of **1** and **2** upon complexation with K^+, Ag^+, Pb^{2+}, Hg^{2+}, Cd^{2+}, Pd^{2+}, Zn^{2+}, Na^+, and Li^+. In the case of **1**, only the addition of K^+ produced perceptible changes in the cyclic voltammograms (CVs) recorded in a 1:1 mixture of CH_2Cl_2 and MeCN at 298 K, whereas receptor **2** only produced observable changes in the CVs upon addition of $AgPF_6$ in accordance with the results obtained from the UV−vis and ^{1}H NMR spectroscopic investigations.

The progressive addition (Figure 3a) of KPF_6 to a solution of the receptor **1** in CH_2Cl_2/MeCN (1:1) at 298 K resulted in a small anodic shift of the first oxidation potential associated with the MPTTF unit, whereas the second oxidation potential was unaffected by the presence of KPF_6. These results can be explained as follows: addition of KPF_6 to a solution of **1** leads to the formation of the **1**•K^+ complex; after the first oxidation of the MPTTF unit, decomplexation takes place caused by Coulombic repulsion between the mono-oxidized $MPTTF^{\bullet+}$ unit and K^+. Consequently, the second oxidation of the $MPTTF^{\bullet+}$ unit in the mixture of uncomplexed receptor $\mathbf{1}^{\bullet+}$ and uncomplexed K^+ takes place at the same potential as that of the second oxidation of **1**.

A more distinct response in the CVs of receptor **2** upon addition of Ag^+ was observed. In contrast to the formation of the **1**•K^+ complex, the kinetics for the dissociation of the **2**•Ag^+ complex were found (Figure 3b) to be slow on the CV time scale, and both complexed and uncomplexed species can be observed in the CVs recorded in CH_2Cl_2/MeCN (1:1) at 298 K. Thus, the addition of between 0 and 1 molar equiv of $AgPF_6$ to a solution of the receptor **2** allows the oxidation potential for both the free receptor **2** (anodic peak potential: $E_1^{ox} = +0.18$ V) and the complex **2**•Ag^+ ($E_1^{ox} = +0.34$ V) to be determined.

Therefore $\Delta E_1^{ox} = +0.16$ V, which to the best of our knowledge is one of the highest values observed so far for cation responsive receptors based on TTF. The second oxidation potential of **2** was only slightly affected by the addition of $AgPF_6$ indicating that the mono-oxidized receptor $\mathbf{2}^{\bullet+}$ has a much lower affinity toward Ag^+. Simulation of the electrochemical titration data using DigiSim3.05 (BAS Inc.[14]) provided a K_a value of 2000 M^{-1} (±20%) for the formation of the **1**•K^+ complex. Owing to the essentially irreversible formation of the **2**•Ag^+ complex, the simulations did not allow for the evaluation of the equilibrium constant for its formation. However, good agreement between the experimental and the simulated data was obtained for values of K_a larger than approximately 10 000 M^{-1}. When considered in concert, the electrochemical investigations support the spectroscopic analyses and provide further evidence that **1** and **2** are highly selective toward K^+ and Ag^+, respectively.

In summary we have designed and synthesized two new redox-active MPTTF based receptors and demonstrated how small modifications in the dibenzo crown ether ring can have a huge impact on the selectivity toward cations. This finding is undoubtedly not unimportant when it comes to the future design of redox-active molecular receptors based on TTF and crown ethers.

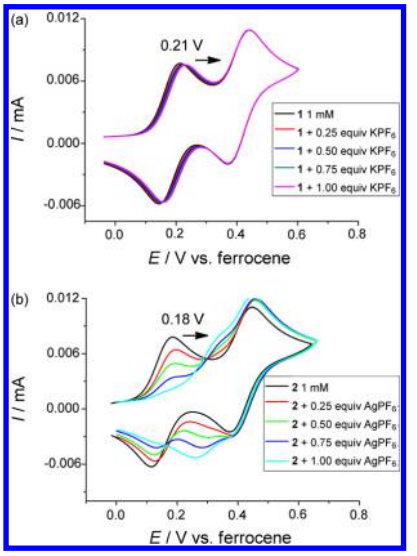

Figure 3. (a) CVs of the receptor **1** (1.0 mM) recorded in a 1:1 mixture of CH_2Cl_2 and MeCN at 298 K by adding in increasing quantities of a concentrated MeCN solution of KPF_6. (b) CVs of the receptor **2** (1.0 mM) recorded in a 1:1 mixture of CH_2Cl_2 and MeCN at 298 K by adding increasing quantities of a concentrated MeCN solution of $AgPF_6$. (The potentials were referred to ferrocene, the supporting electrolyte was n-Bu_4NPF_6, and the scan rate was 200 mV s^{-1}.)

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Supporting Information Available. Experimental procedures for the synthesis of **1**, **2**, **6**−**9**, **11**, and **12**; spectroscopic characterization of **1** and **2**; description of titration experiments; and description of electrochemical measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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