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Electrochemical M^{2+} recognition by an amidopyridyl-tetrathiafulvalene derivative†

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Received (in Montpellier, France) 19th February 2008, Accepted 18th April 2008
First published as an Advance Article on the web 7th May 2008
DOI: 10.1039/b802726a

A tetrathiafulvalene-based redox-responsive receptor incorporating amide and pyridyl coordinating units exhibits an original multi-wave electrochemical recognition behaviour towards Cd(II).

The tetrathiafulvalene (TTF) unit constitutes a key system for the construction of redox-responsive ligands.[1] This ability results from remarkable electronic properties, this system being easily oxidized in two successive one-electron steps into a stable cation-radical (E^1_{ox}) and a dication (E^2_{ox}). Depending on the binding site which is covalently associated to the TTF skeleton, the resulting receptors are able to electrochemically sense cations[2,3] or anions.[4] Most of these receptors involve a binding site made of a crown-ether cavity[2] or a coordinating acyclic domain.[3,4b–f] On the other hand, important synthetic efforts have been recently made in attaching coordinating pyridyl unit(s) to the TTF skeleton, in order to obtain hybrid organic–inorganic materials with rich solid-state physical properties.[5] In particular, conjugation of amide and pyridyl units for tuning of the solid-state organization of TTF-based materials has been described.[5d] Nevertheless, it is only very recently that metal binding studies and the exploration of solution sensing properties have been conducted with TTF–pyridine assemblies.[3a–c,h]

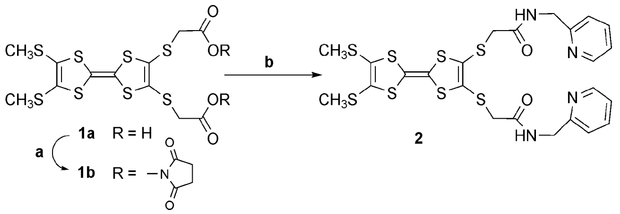
Following these considerations, we have designed the TTF-based ligand **2** incorporating pyridyl and amide binding groups, which are located in respective positions in order to operate in a cooperative way for metal cation binding. Herein, we report on the synthesis of ligand **2** and demonstrate that this receptor undergoes an original and highly effective electrochemical recognition process for the detection of transition metal cations (Cd^{2+}, Ni^{2+}, Co^{2+}). The X-ray structure of one of the corresponding metal complexes is also provided.

Target receptor **2** was prepared from TTF diacid derivative **1a** and the corresponding NHS-activated ester **1b**, both synthesized according to the literature[4b] (Scheme 1). Reaction of **1b** with 2-(aminomethyl)pyridine at room temperature for 2 h produced **2** in 70% yield.

The binding ability of receptor **2** in the presence of Cd^{2+} was first evidenced by ^1H NMR spectroscopy. Titration experiments were carried out in $CDCl_3$–CD_3CN (1 : 1) with cadmium perchlorate. Protons of both pyridyl groups are shifted to a lower field upon addition of $Cd(ClO_4)_2$, as expected from the contribution of these fragments to the cation complexation process. Moreover, the resulting titration curve (Fig. 1, S1†) exhibits a plateau for 1 equivalent of added cation, in accordance with a 1 : 1 stoichiometry for the corresponding complex. An average K° value of $10^{4.9\pm0.1}$ L mol^{-1} ($CDCl_3$–CD_3CN, 20 °C) was determined from the different ^1H NMR signals by using the EQNMR program.[6]

The strong binding affinity of **2** towards Cd^{2+} could also be checked by UV–Vis spectroscopy in CH_2Cl_2–CH_3CN (1 : 1) (Fig. S2†), from which the binding constant K° could be determined using the Benesi–Hildebrand method[7] at 264 nm ($K^\circ = 10^{4.9\pm0.06}$ L mol^{-1}; CH_2Cl_2–CH_3CN, 20 °C).

Finally, the recognition properties of the redox-active receptor **2** were also evaluated by cyclic voltammetry (CV) in CH_2Cl_2–CH_3CN (1 : 1) (Bu_4NPF_6 (0.1 M)). Compound **2** exhibits two reversible one electron redox processes upon oxidation to the radical cation ($E^1_{ox} = 0.59$ V *vs.* Ag/AgCl) and the dication ($E^2_{ox} = 0.87$ V) (Fig. 2). As usually observed with TTF-based redox-responsive ligands,[2] binding of a cation results in an anodic shift of the first oxidation potential ($\Delta E^1_{ox} = +60$ mV). This experimental observation results from the decrease of the π-donating ability following the binding of a guest cation near to the TTF core. On the other hand, the second oxidation potential E^2_{ox} of TTF-based redox-responsive ligands usually remains constant upon addition of a metal cation,[2] which is classically attributed to metal expulsion, resulting from repulsive through-space electrostatic interactions with TTF^{2+}. Conversely, only recently was described



Scheme 1 *Reagents and conditions:* (a) ref. 4*b*; (b) 2-(aminomethyl)pyridine, THF, rt, 2 h, 70%.

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† Electronic supplementary information (ESI) available: ^1H NMR, UV–Vis and electrochemical titration studies for compound **2** with Cd^{2+}, CV titration of **2** with Ni^{2+}. Crystallographic data for the structure reported in this paper in CIF format: CCDC 653209. See DOI: 10.1039/b802726a

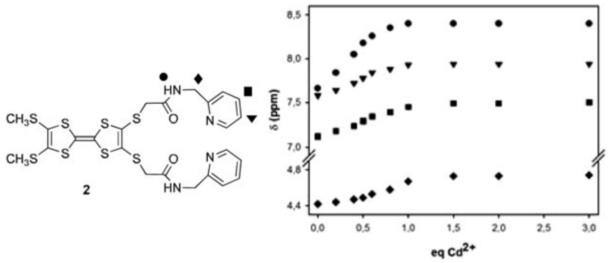


Fig. 1 ^{1}H NMR titration curves of **2** (0.022 mol L^{-1} in CDCl$_3$–CD$_3$CN 1 : 1) upon addition of Cd(ClO$_4$)$_2$.

moderate positive shifts of E^2_{ox} upon addition of Pb^{2+} in the case of various TTF–π–pyridine systems.[3a,b,h] In those cases, the pyridyl binding site is connected through a conjugated linker to the TTF core. We also very recently reported on a π-extended tetrathiafulvalene ligand which presents a remarkable positive shift of E^2_{ox},[3c] which accounts for the stability of the metal complex even though the redox unit is doubly oxidized. This result illustrates the effect of a π-extension of the TTF backbone, which induces a lowering of coulombic repulsion between the oxidized redox unit and the metal cation. A very similar electrochemical behaviour is actually observed with compound **2**, for which the second redox potential (E^2_{ox}) is surprisingly shifted by as much as +110 mV upon addition of Cd(ClO$_4$)$_2$ (Fig. 2). A remarkable two-wave behaviour is even observed for the second redox process, associated with a Cd^{2+} binding which still exists at the dication $\mathbf{2}^{2+}$ stage.

The shape of the voltammogram can be rationalized thanks to the square scheme presented in Scheme 2, where K°, K^+ and K^{2+} correspond to the binding constants between the metal cation and the receptor in various redox states.

From these electrochemical data and by using the DIGISIM 3.0 simulation program (BAS) (ESI†),[8] the following binding constants could be evaluated: K° = 10^5, K^+ = 10$^{4.4}$, and K^{2+} = 10$^{1.6}$ L mol^{-1} (Fig. S3†). A similar CV behaviour (Fig. S4†) was observed by introducing nickel perchlorate (ΔE^1_{ox} = +50 mV; ΔE^2_{ox} = +60 mV) and, to a lower extent, with cobalt perchlorate (ΔE^1_{ox} = +50 mV; ΔE^2_{ox} = +10 mV).

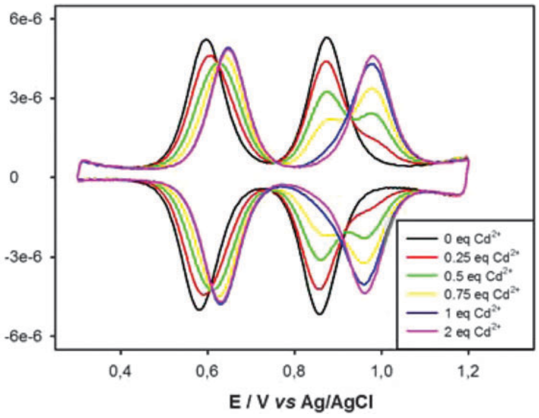
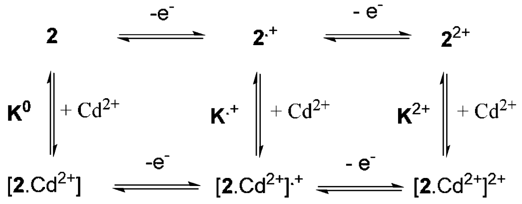


Fig. 2 Deconvoluted cyclic voltammogram of compound **2** (10^{-3} M) in the presence of increasing amounts of Cd(ClO$_4$)$_2$; CH$_2$Cl$_2$–CH$_3$CN (1 : 1); Bu$_4$NPF$_6$ (0.1 M); 100 mV s^{-1}; Pt working electrode, diameter 1 mm.



Scheme 2 Square scheme for the electrochemical titration of **2** in presence of Cd^{2+}.

Single crystals of the Cd(II) complex could be grown by slow diffusion of pentane vapours to a dichloromethane–acetonitrile solution of **2** in presence of Cd(ClO$_4$)$_2$. The resulting X-ray crystal structure is shown in Fig. 3. A 1 : 1 stoichiometry between **2** and Cd^{2+} is observed, as well as a solvent molecule (**2**-Cd(ClO$_4$)$_2$,CH$_3$CN). The metal cation presents an octahedral coordination. Two coordinating nitrogen atoms belonging to both pyridyl groups (Cd–N 2.288(3)–2.302(3) Å) are completed by two oxygen atoms of the carbonyl groups (Cd–O 2.311(3)–2.315(3) Å), one nitrogen atom of an acetonitrile molecule (Cd–N 2.330(5) Å) and one oxygen atom of a perchlorate anion (Cd–O 2.445(3) Å) (the second perchlorate anion does not participate in metal binding). It is worth noting that mean planes of both coordinating pyridyl rings are nearly coplanar and parallel to the TTF skeleton, with an interplanar (pyridyls *vs.* TTF planes) distance of *ca.* 4.8 Å, which is therefore also the approximate distance between Cd^{2+} and the TTF mean plane (Cd–C7 = 4.800(4), Cd–C8 = 4.854(4), Cd–S8 = 5.020(2), Cd–S7 = 5.060(2) Å). As far as we know, such a location of the metal cation, shifted regarding the TTF plane, has not been encountered with other TTF–pyridyl complexes, and is presumably responsible for the peculiar electrochemical behaviour observed for **2** in presence of

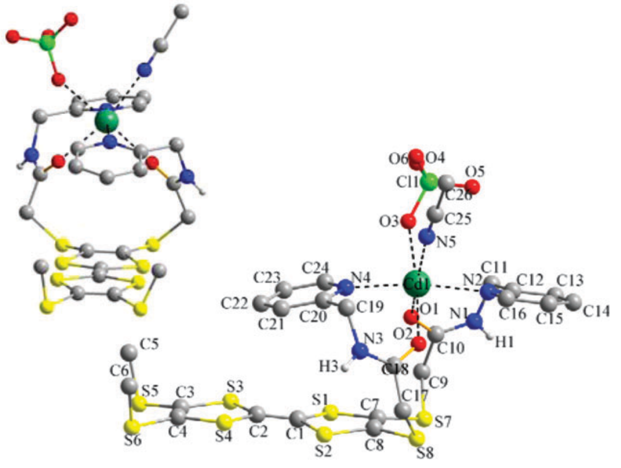


Fig. 3 Molecular structure along two directions, and atom numbering scheme for **2**-Cd(ClO$_4$)$_2$,CH$_3$CN with selected bond distances (Å). H-atoms (except N–H amide) and one ClO$_4^-$ anion are omitted for clarity. C1–C2 1.327(7), C7–C8 1.340(6), C3–C4 1.34(1), C2–S4 1.754(6), C2–S3 1.751(6), C1–S2 1.761(5), C1–S1 1.755(5), C4–S4 1.735(9), C3–S3 1.752(9), C8–S2 1.737(5), C7–S1 1.762(5), C9–S7 1.822(5), C17–S8 1.812(5), C10–O1 1.234(5), C18–O2 1.239(5), C10–N1 1.318(5), C18–N3 1.319(5), C11–N1 1.450(6), C19–N3 1.461(6), Cd1–N2 2.302(3), Cd1–N4 2.288(3), Cd1–N5 2.330(5), Cd1–O1 2.311(3), Cd1–O2 2.315(3), Cd1–O3 2.445(3).

transition metal cations. The spatial arrangement is such that the cation is locked in a rigid environment (preventing expulsion, even in the TTF^{2+} state), and is located directly over the redox unit, leading to an optimized through-space interaction with the redox-active unit.

In conclusion, we have described an amidopyridyl-TTF redox-responsive system **2** and we have studied its solution binding properties towards transition metal cations (CV, ^{1}H NMR) as well as its solid-state characteristics through X-ray diffraction studies on a corresponding complex. An original electrochemical (CV) behaviour was observed, manifested by strong positive shifts of both oxidation potentials of **2** in presence of Cd^{2+}. In particular, the observation of a remarkable two-wave behaviour for the second redox system accounts for the high stability of the complex, even when ligand **2** is oxidized to the dication, which constitutes a very unusual behaviour among TTF-based sensors.

Experimental

Synthesis of 2: Tetrathiafulvalene derivative **1b** (0.67 g, 1 mmol) was dissolved in dry THF (30 mL), and degassed with N_2 for 10 min. A solution of 2-(aminomethyl)pyridine (0.119 g, 1.1 mmol) in dry THF (10 mL) was then added. The reaction mixture was stirred during 3 h and the solvent was removed in vacuum. The resulting solid was dissolved in CH_2Cl_2, washed with water, dried over $MgSO_4$ and purified by silica gel column chromatography using THF to give **2** as an orange solid in 70% yield.

Spectroscopic data for **2**: orange solid; mp = 150 °C; ^{1}H NMR ($CDCl_3$): 2.4 (s, SCH_3, 6H), 3.6 (s, SCH_2, 4H), 4.55 (d, CH_2NH, 4 H), 7.16 (m, $=$CH, 1H), 7.22 (m, $=$CH, 1H), 7.62 (m, $=$CH, 1H), 7.79 (m, NH, 1H), 8.49 (m, N$=$CH, 1H); ^{13}C NMR ($CDCl_3$): 19.1 (SCH_3), 39.1 (SCH_2), 45.0 ($NHCH_2$), 108.9, 112.9 (C$=$C centrals), 127.4, 127.9, 121.9, 122.4, 148.9, 149.1, 156.2 ($C{=}C_{\text{laterals and pyridine}}$), 167.0 (C$=$O). Anal. for $C_{24}H_{24}N_4O_2S_8$: Found (Calcd.): C, 43.89 (43.88), H, 3.71 (3.68), N, 8.51 (8.53), O, 4.75 (4.87), S, 38.92 (39.04)%. HRMS-EI(+): *m*/*z*: calcd. for $C_{24}H_{24}N_4O_2S_8$: 655.9665; found: 655.9679 [$M^{+\bullet}$].

Crystal data for 2-$Cd(ClO_4)_2$,CH_3CN ($C_{26}H_{27}CdCl_2$-$N_5O_{10}S_8$): M = 1009.31, monoclinic, $P2_1/c$, a = 20.590(6), b = 13.4517(8), c = 14.543(1) Å, β = 103.64(2)°, V = 3914.4(12) Å^3, Z = 4, D_{calc} 1.713, T = 293 K, μ = 1.18 mm^{-1}, $2\theta_{\max}$ = 56°, 9792 measured reflns, 6287 unique reflns with $I/\sigma(I) > 2$ (R_{int} = 0.017), $R(F)$ = 0.048 (488 parameters), w$R2(F2)$ = 0.149 (all data).

Data collection was carried out on a Bruker Kappa CCD diffractometer, graphite-monochromated, MoKα radiation (λ = 0.71073 Å). The structure was solved by direct methods, and refined by full-matrix least-squares routines against F^2 using the Shelxl97 package anisotropic thermal motion parameters for all non-H atoms. The hydrogen atoms were treated with a riding model. A statistical disorder affects two oxygen atoms of the ClO_4^- anion which is non bonded to Cd^{2+}, each atom being split over two positions with a half occupation rate.

Acknowledgements

This work has been partly supported by the French–Algerian Tassili programme 08MDU730. Dr E. Levillain is acknowledged for his help in running the electrochemical simulation study and M.S. thanks the Institut Universitaire de France (IUF) for financial support.

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