A novel redox-active calix[4]arene-tetrathiafulvalene dyad

Research Article

Bang-Tun Zhao[1*], Xiao-Min Zhu[2], Qi-Ming Peng[2],
Zhen-Ning Yan[2], Franck Le Derf[3], Marc Sallé[3]

[1]*Department of Chemistry, Luoyang Normal University,
Luoyang 471022, P. R. China*

[2]*Department of Chemistry, Zhengzhou University,
Zhengzhou 450001, P. R. China*

[3]*Laboratoire MOLTECH-Anjou,UMR CNRS 6200,
Université d'Angers, F-49045 Angers, France*

Abstract: A novel redox-active calix[4]arene-TTF **5** was prepared by the reaction of *p-tert*-butylcalix[4]arene **4** with the tosylated TTF **3** in the presence of cesium fluoride. The structure of the dyad **5** was identified by X-ray diffraction analysis, and the preliminary electrochemical properties of **5** were investigated by cyclic voltammetry (CV), for which two reversible one-electron waves were observed. Moreover, the UV-vis absorption spectra studies show that the dyad **5** undergoes progressive oxidation at the TTF moiety in presence of increasing amounts of Cu^{2+} or Hg^{2+}.

Keywords: *Calix[4]arene • Tetrathiafulvalene • Crystal structure • Cyclic voltammetry*

© Versita Sp. z o.o.

1. Introduction

In 1997, Regnouf-de-Vains *et al*. designed a novel redox-active receptor based on covalent association of calix[4]arene and tetrathiafulvalene (TTF) units, in which the latter was grafted on the upper rim of the calixarene *via* an imine bond [1]. Since then, various calixarene-TTF derivatives have been prepared with the objective to associate in a single molecule, the well-established host properties of the calixarene platform to the redox characteristics of the TTF unit; the assembly can potentially act as a redox probe [2] for sensing a guest binding. On this ground, several systems have been designed, for which the TTF units are introduced to either lower or upper rims of the calixarene framework [3-11]. Beside calix[4]arene, alternative polyaromatic scaffolds have been substituted by electroactive TTF units such as a thiacalix[4]arene [12,13] or resorcin[4]arene [14] units. Several of these electroactive calixarene-TTF architectures have displayed sensing properties toward cationic [6-8] or anionic [4,9,11] species. As part of our

ongoing research program, based on the design and the preparation of novel calixarene-TTF assemblies for sensing applications; we hereby present the synthesis of a novel calixarene-TTF derivative bearing a polyether linker, which is prone to contribute to a cation binding process, as well as its characterization including crystal structure determination, electrochemical properties and recognition properties for metal ions.

2. Experimental procedure

All reactions were carried out under nitrogen atmosphere, and all dry solvents were prepared according to standard procedures. Melting points are uncorrected and were determined using a Boetius Block apparatus (China). The $^1H(^{13}C)$ NMR spectra were recorded at Bruker DPX 400 MHz, and the IR spectra were measured on an FT-IR spectrometer Nicolet Avata 350 in KBr. Mass spectra were measured using ESI technique on Bruker Esquire 3000 spectrometer. Elemental analyses were measured

on Carlo-Erba 1106 instruments. X-Ray crystallographic data for **5** were obtained using a Bruker SMART APEX II CCD diffractometer equipped with graphite monochromated Mo Kα radiation (λ = 0.71073 Å) at 293 K. The structure was solved by direct methods using SHELXS-97 and refined using SHELXL-97 by full-matrix least-squares methods on F^2 [15,16]. Hydrogen atoms were located from expected geometry and were isotropically refined by riding model. All non-hydrogen atoms were refined anisotropically except those of the disordered fragments. The φ-ω scan was used for absorption correction. Cyclic voltammetry (CV) experiments were performed on a CHI620C electrochemistry workstation in a three-electrode system served as Pt working electrode (2 mm, diameter), with Ag/AgCl and platinum wire acting as reference and counter electrodes, respectively. The UV absorption spectra were measured on a UV-3010 UV–vis spectrophotometer.

2.1. Synthesis of 2,3-bis[2-(2-hydroxyethoxy) ethylsulfanyl]-6,7-bis(methylthio) tetrathiafulvalene (2) [17]

The TTF derivative **1** (1.13 g, 2.42 mmol) [18] was dissolved in THF (50 mL) and degassed with N_2 for 30 min. A solution of CsOH•H_2O (0.88 mg, 5.32 mmol) in dry methanol (2 mL) was added in one portion, producing a darkening of the solution. After stirring for an additional 30 min, a solution of 2-(2-iodoethoxy) ethanol (3.14 g, 14.52 mmol) in THF (10 mL) was added. The reaction mixture was stirred for 24 h, and the solvent was removed under reduced pressure. The resulting orange solid was dissolved in methylene chloride, washed with water several times, and dried over MgSO$_4$. Concentration *in vacuo* and purification by a silicagel column chromatography (methylene chloride: ethyl acetate = 2:1) afforded **2** as an orange solid in 45 % yield. Mp: 57°C (Lit. [17] mp 56°C). ^{1}H NMR (CDCl$_3$, ppm): δ: 3.74 (br, s, 4 H, OCH$_2$), 3.69 (t, J = 6.0 Hz, 4 H, OCH$_2$), 3.59 (t, J = 4.4 Hz, 4 H, OCH$_2$), 3.05 (t, J = 6.0 Hz, 4 H, SCH$_2$), 2.67 (br, s, 2 H, OH), 2.43(s, 6 H, SCH$_3$). Lit. ^{1}H NMR (CDCl$_3$, ppm): δ: 3.72 (t, J = 4.0 Hz, 4 H, OCH$_2$), 3.67 (t, J = 6.0 Hz, 4 H, OCH$_2$), 3.56 (t, J = 4.0 Hz, 4 H, OCH$_2$), 3.02 (t, J = 6.0 Hz, 4 H, SCH$_2$), 2.40(s, 6 H, SCH$_3$).

2.2. Synthesis of 2,3-bis[2-(2-tosyloxyethoxy) ethylsulfanyl]-6,7-bis(methylthio) tetrathiafulvalene (3)

To a solution of **2** (0.58 g, 1.09 mmol) in methylene chloride (30 mL) was added tosyl chloride (0.46 g, 2.39 mmol). The solution was cooled to 0°C and NEt$_3$

(2 mL, excess) was added dropwise. The reaction mixture was stirred at room temperature under N_2 for 20 h. The organic phase was washed with water, dried over MgSO$_4$, and evaporated to yield an oil residue, which was chromatographied on a silica column using methylene chloride/petroleum ether (10:1, V:V) to give **3** as red-orange sticky oil in 89% yield. ^{1}H NMR (CDCl$_3$, ppm): δ: 7.80 (d, J = 8.0 Hz, 4 H, ArH), 7.35 (d, J = 8.0 Hz, 4 H, ArH), 4.16 (t, J = 4.6 Hz, 4 H, TsOCH$_2$), 3.68 (t, J = 4.4 Hz, 4 H, OCH$_2$), 3.60 (t, J = 6.6 Hz, 4 H, OCH$_2$), 2.92 (t, J = 6.4 Hz, 4 H, OSH$_2$), 2.45(s, 6 H, ArCH$_3$), 2.43(s, 6 H, SCH$_3$).

2.3. Synthesis of calix[4]arene-tetrathiaful-valene (5)

A suspension of *p-tert*-butylcalix[4]arene **4** (0.27 g, 0.41 mmol) and CsF (0.31 g, 2.07 mmol) in dry CH$_3$CN (100 mL) was refluxed for 1 h. Then a solution of tosylated TTF **3** (0.35 g, 0.41 mmol) in dry CH$_3$CN (100 mL) was slowly added over a 8 h period. The mixture was refluxed for 24 h before the solvent was removed under reduced pressure. The residue was dissolved in CH$_2$Cl$_2$ (30 mL) and brine was added. The organic layer was separated and dried over MgSO$_4$. The crude product obtained after evaporation of the solvent was purified on a silica column using methylene chloride/petroleum ether (2:1, V:V) to give **5** as orange powders in 36% yield. Mp: 155-157ºC. ^{1}H NMR (400 MHz, CDCl$_3$, ppm): δ: 7.44 (s, 2 H, OH), 7.05 (s, 4 H, ArH), 6.83 (s, 4 H, ArH), 4.33 (d, J = 12.96 Hz, 4 H, ArCH$_2$Ar), 4.12 (t, J = 4.6 Hz, 4 H, ArOCH$_2$), 4.06 (t, J = 4.5 Hz, 4 H, ArOCH$_2$C**H**$_2$), 3.94 (t, J = 6.56 Hz, 4 H, OC**H**$_2$CH$_2$S), 3.30 (d, J = 13.00 Hz, 4 H, ArCH$_2$Ar), 3.12 (t, J = 6.56 Hz, 4 H, OCH$_2$C**H**$_2$S), 2.42 (s, 6 H, SCH$_3$), 1.28 (s, 18 H, C(CH$_3$)$_3$), 0.98 (s, 18 H, C(CH$_3$)$_3$). ^{13}C NMR (150 MHz, CDCl$_3$): δ: 150.6, 149.6, 147.0, 141.4, 132.8, 128.7, 127.8, 127.4, 125.9, 125.6, 125.1, 111.1, 110.6, 75.2, 70.2, 69.9, 38.2, 35.3, 33.9, 33.8, 31.7, 31.6, 31.4, 31.2, 31.0, 29.7, 29.2. IR (KBr cm^{-1}): υ: 3434.9, 2961.9, 2917.6, 2865.5, 1635.0, 1485.5, 1362.7, 1200.7, 1123.3, 1094.6, 1052.2, 863.1, 811.0, 774.4. MS-ESI: m/z calculated: 1148.34; found: 1148 (M$^+$), 1281 (M+Cs)$^+$. Anal. Calcd for C$_{60}$H$_{76}$S$_8$O$_6$, C, 62.70; H, 6.67; S, 22.27. Found: C, 62.45; H, 6.84; S, 22.14.

2.4. Crystallographic study

X-Ray data for **5**: C$_{62}$H$_{79}$NO$_6$S$_8$, M = 1190.74 g mol^{-1}, Monoclinic, space group C2/c, a = 52.33(4) Å, b = 11.223(8) Å , c = 23.969 (17 Å, α = 90º, β = 112.180(9) º, γ = 90º, V = 13037(16) Å^3; Z = 8, Dc =1.213 g cm^{-3}, μ = 0.321 mm^{-1}, F(000) = 5072, crystal dimensions of 0.23×0.12×0.11 mm. The final refinement

gave R = 0.0794 and Rw = 0.1235 using 12146 independent reflections (θ_{max} = 25.50, 762 parameters). The max. and min. difference peaks and holes are 0.631 and -0.370 e Å^{-3}, respectively.

3. Results and discussion

3.1. Design and synthesis

The synthetic route to target calix-TTF **5** is outlined in Scheme 1. A solution of bis(methylthio)-bis(2-cyanoethylthio) TTF **1** [18], obtained by cross-coupling of 4,5-bis(2-cyanoethylthio)-1,3-dithio-2-one and the 4,5-bis(methylthio)-1,3-dithio-2- thione in triethyl phosphite, was transformed into the diol **2** by treatment with two equiv. of CsOH in methanol and subsequent realkylation with 2-(2-iodoethoxy)ethanol (45% yield). The key TTF derivative **3** was synthesized by a classical tosylation procedure in 89% yield [19]. The final coupling reaction between *p-tert*-butylcalix[4]arene **4** and the tosylated TTF **3** was carried out in refluxing acetonitrile in the presence of cesium fluoride, used both as a weak base and as a cyclization template. In this way, the target compound **5**

was obtained in reasonable yield of 36%. The ^{1}H NMR spectrum of compound **5** shows two singlets for both the Bu^t and Ar-H protons, along with a pair of doublets assigned to diastereotopic bridging methylene protons (ArCH$_2$Ar) [20], which indicate a cone conformation for **5** in solution.

3.2. X-Ray structure

Single crystals of compound **5** were obtained by slow evaporation of a chloroform-methanol mixture at *rt*, and studied by X-ray diffraction methods. As seen from Fig. 1A, the calixarene framework adopts a cone conformation, in which one acetonitrile molecule is encapsulated, and the TTF unit is nearly planar. There exist two intramolecular hydrogen bondings of O2-H2···O1(d(O1···H2) = 2.01 Å; ∠ O2—H2···O1 = 170°) and O4—H4A···O3 (d(H4A···O3) = 2.22 Å; ∠ O4—H4A···O3 = 143°). Moreover, intermolecular weak S···S interactions, with a distance of 3.823 Å [21], link adjacent TTF frameworks to form a 1D chain along *b*-direction (Fig. 1B).
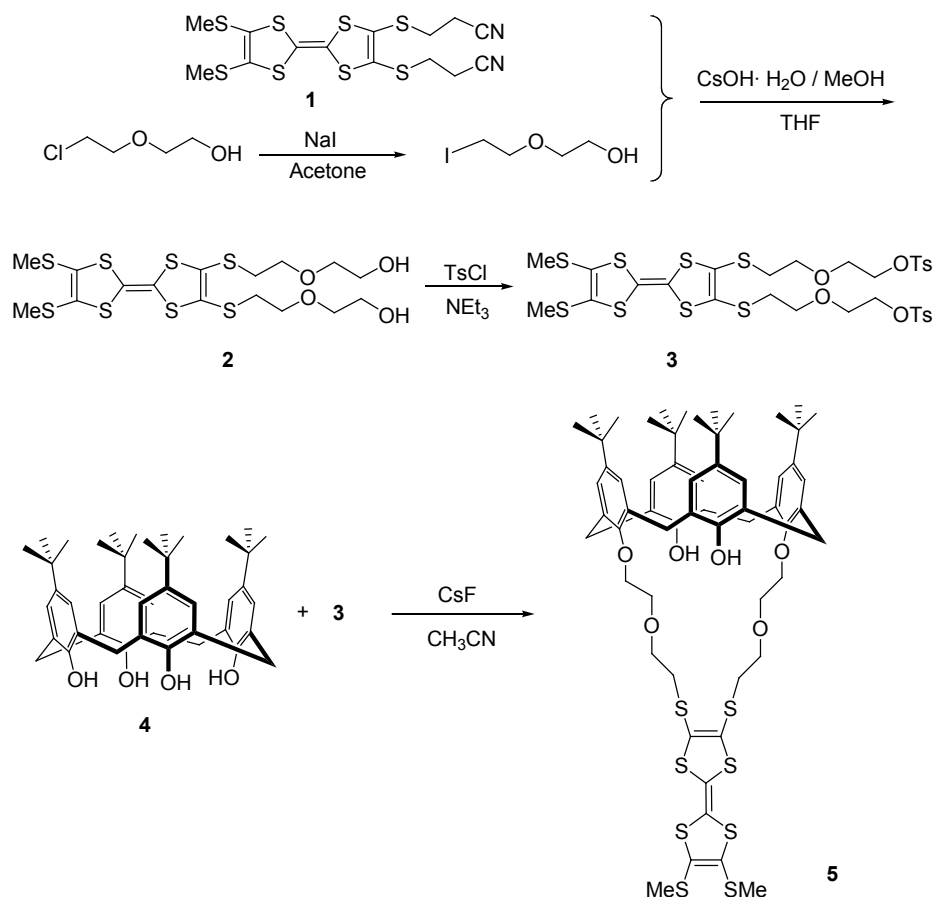
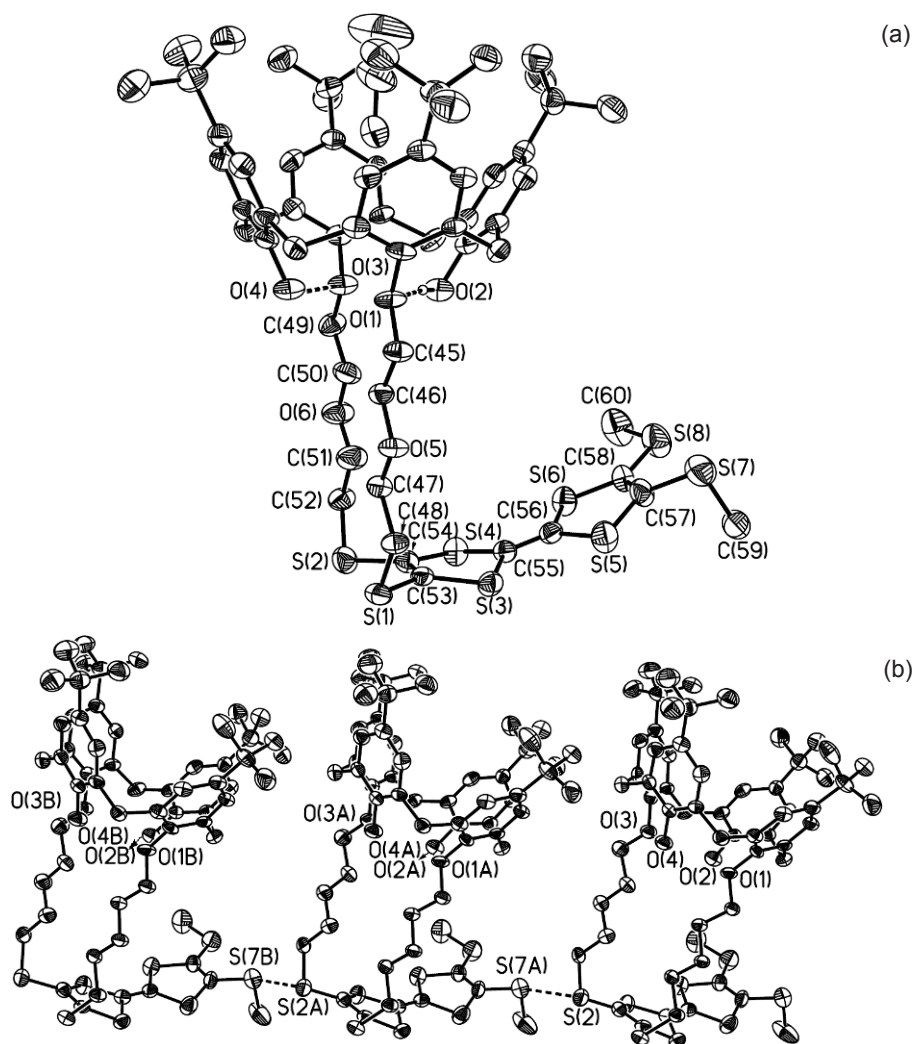**Scheme 1.** Synthetic route to the preparation of calix[4]arene-tetrathiafulvalene dyad **5**.

Figure 1. (a) Molecular structure of **5** (All hydrogen atoms and disordered carbon atoms of tert-butyl groups are deleted for clarity); (b) 1D chain formed by weak S⋯S interactions along *b*-direction.

3.3. Electrochemical behavior

The electrochemical properties of calix[4]arene-TTF **5** together with the parent 2,3,6,7-tetrakis(methylthio) tetrathiafulvalene (TTF(SMe$_3$)$_4$) were carried out on a CHI620 electrochemistry workstation in a dichloromethane-acetonitrile (1/1, v/v) mixture. The parent TTF(SMe)$_4$ is well known to undergo two successive reversible one-electron redox processes leading respectively to cation-radical and dicationic species at $E^{1/2}_1$ = 0.53 V and $E^{1/2}_2$ = 0.84 V (*vs.* Ag/AgCl), respectively. As expected from the electrochemical inertness of the calix[4]arene platform [22], only the TTF redox signature is observed for compound **5**, which undergoes the expected two reversible redox waves at $E^{1/2}_1$ = 0.56 V and $E^{1/2}_2$ = 0.84 V (*vs.* Ag/AgCl), corresponding to the successive formation of the stable TTF/TTF^{-+} and TTF^{-+}/TTF^{2+},

respectively (Fig. 2). The higher first $E^{1/2}_1$ potential (0.56 V) for compound **5** (0.53 V for the parent TTF(SMe)$_4$) may be ascribed to two 2-(oxyethoxy)ethylsulfanyl substituents (-OCH$_2$CH$_2$OCH$_2$CH$_2$S-) on TTF framework, however, the second $E^{1/2}_1$ potential (0.84 V) basically remains unchanged (0.84 V for the parent TTF(SMe)$_4$).

3.4. UV-Vis titration for metal ions

The recognition properties of the redox-active dyad **5** were evaluated by UV-Vis spectroscopy (CH$_2$Cl$_2$/MeCN 1:1). As can be seen from Fig. 3, the absorption spectra of compound **5** exhibits intense absorption bands at λ < 380 nm, with extinction coefficients on the order of 10^4 dm^3 mol^{-1} cm^{-1}. While 1 equiv. Cu^{2+} and Hg^{2+}, available as the perchlorate salts, were added to the solution of **5**, the UV-vis absorption spectrum displayed dramatic changes, whereas no obvious changes were
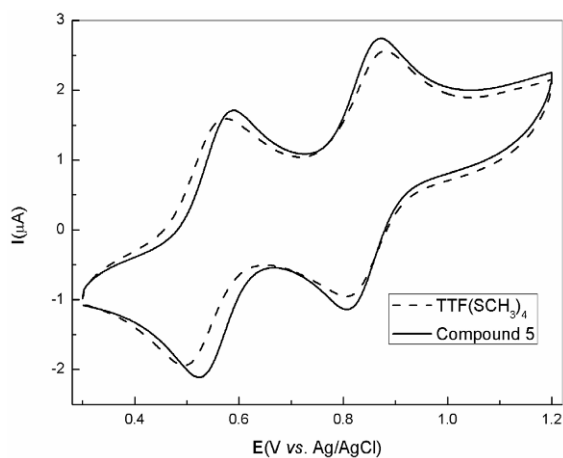
Figure 2. Cyclic voltammetry of compound **5** and parent TTF(SMe$_3$)$_4$ (0.5 mM) in CH$_2$Cl$_2$/MeCN(1/1), Bu$_4$NPF$_6$(0.1 M), v = 100 mV s^{-1}, Pt(φ 2 mm), vs. Ag/AgCl.
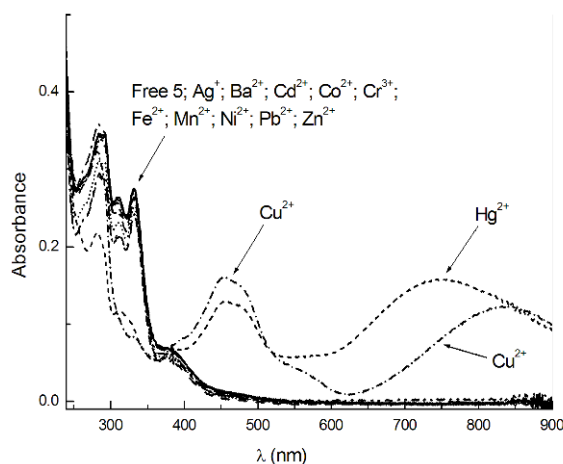
Figure 3. Absorption spectra of **5** (1.0×10^{-5} M in CH$_2$Cl$_2$/CH$_3$CN(1:1) upon addition of 1 equiv. of different metal ions.

Figure 4. Absorption spectra of **5** (1.0×10^{-5} M in CH$_2$Cl$_2$/CH$_3$CN(1:1) upon addition of different equiv. Cu^{2+} ions: 0.0~0.8 equiv. (a); 0.8~2.0 equiv. (b).

observed upon addition of other metal ions such as Ag$^+$, Ba^{2+}, Cd^{2+}, Ba^{2+}, Co^{2+}, Cr^{3+}, Fe^{2+}, Mn^{2+}, Ni^{2+}, Pb^{2+}, Zn^{2+}. These changes are assigned to the progressive oxidation of the TTF moiety in presence of increasing amounts of Cu^{2+} or Hg^{2+}. Examples of TTF derivatives which are oxidized to the cation-radical state in presence of Cu(II) salts are already known [23]. Nevertheless, quite surprisingly, we also observed oxidation of the TTF center to the dicationic state. As can be seen from Fig. 4, with the progressive addition of Cu^{2+}, the absorption band of **5** at around λ = 340 nm decays monotonically, and new bands at λ = 455 nm and 840 nm emerge and concomitantly grow up with increasing Cu^{2+} concentration up to 0.8 equiv. There is one isosbestic point at λ = 370 nm. Interestingly, while the addition of Cu^{2+} is pursued from 0.8 to 2.0 equiv., the bands at λ = 455 nm and 840 nm decay gradually, and a new one emerges
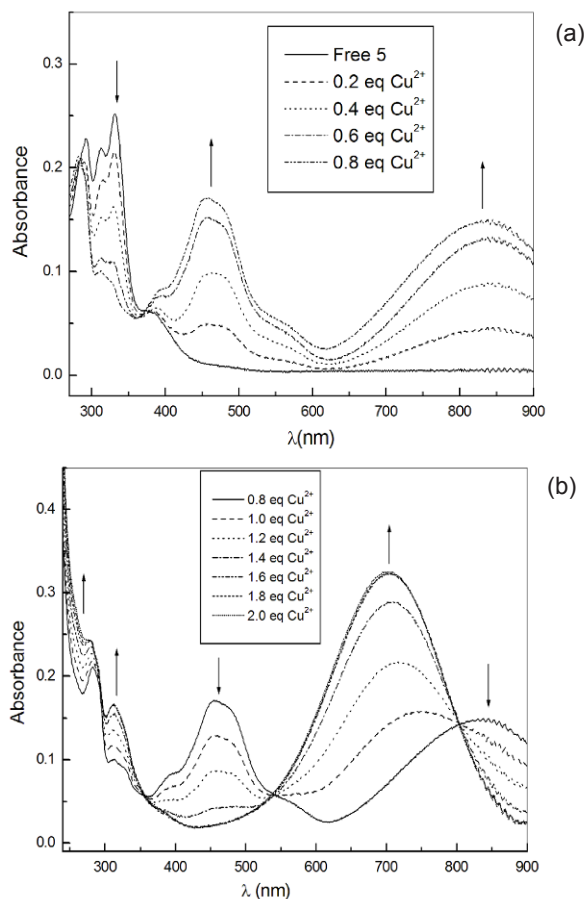
at λ = 710 nm, with four isosbestic points at λ = 290, 355, 540 and 805 nm. Such behavior nicely illustrates the two-step one-electron oxidations of the TTF unit, producing successively a stable radical-cation species **5**$^{\cdot+}$ (λ = 455 nm and 840 nm), and then the dication species **5**$^{2+}$ (710 nm). These values are in accordance with literature data for the cation-radical and the dicationic species obtained from the parent tetramethylsulfanyl-TTF derivative [24]. A similar behavior is observed with addition of Hg^{2+}(Fig. 5), with first a decreasing of the band corresponding to the neutral TTF state (340 nm) and a concomitant appearing of new bands which are assigned to the cation-radical state (455 nm and 840 nm), and then emergence of a band assigned to the dicationic state (720 nm). Based on the UV-vis experimental results, the reaction equations may be deduced as following (M = Cu or Hg) :
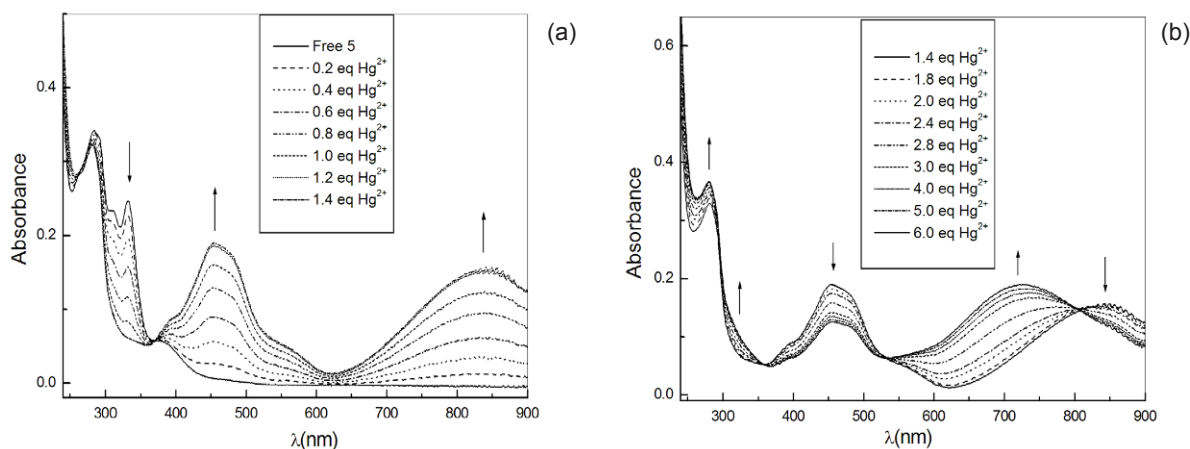
$$5 + M^{2+} = 5^{\cdot+} + M^+ \text{ (I)}$$

$$5^{\cdot+} + M^{2+} = 5^{2+} + M^+ \text{ (II)}$$
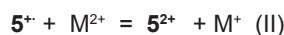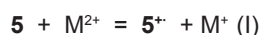
Figure 5. Absorption spectra of **5** (1.0×10^{-5} M in $CH_2Cl_2/CH_3CN(1:1)$ upon addition of different equiv. Hg^{2+} ions: 0.0~1.4 equiv. (a); 1.4~6.0 equiv. (b).

Though no definitive explanation can be made from these preliminary data, a possible explanation lies on a binding contribution of M by receptor **5**, whose effect presumably impacts the redox activity. Further investigation in this direction is under way.

4. Conclusion

In summary, a new redox-active calix[4]arene-TTF dyad **5** was synthesized by the reaction of *p-tert*-butylcalix[4] arene **4** and the tosylated TTF **3** in refluxing acetonitrile. The dyad **5** displayed a cone conformation in both solution and solid state, which were identified by ^{1}H NMR spectrum and X-ray diffraction analysis, respectively. The electrochemical behavior showed that compound **5** undergoes two reversible redox waves and the UV-vis absorption spectra studies illustrates progressive oxidation of the TTF moiety with the successive formation of radical-cation and, very surprisingly, to the dication species in presence of increasing amounts of Cu^{2+} or Hg^{2+}.

Supplementy materials

Crystallographic data for **5** (CCDC-784766) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary materials. Copies of available material can be obtained free of charge on application to the Director, CCDC. 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk)

References

[1] J.B. Regnouf de Vains, M. Sallé, R. Lamartine, J. Chem. Soc., Perkin Trans 2, 2461 (1997)

[2] D. Canevet, M. Sallé, G. Zhang, D. Zhang, D. Zhu, Chem. Commun. 2245 (2009)

[3] B.T. Zhao, M.J. Blesa, N. Mercier, F. Le Derf, M. Sallé, Supramol. Chem. 17, 465 (2005)

[4] B.T. Zhao, M.J. Blesa, N. Mercier, F. Le Derf, M. Sallé, New .J. Chem. 29, 1164 (2005)

[5] B.T. Zhao, M.J. Blesa, N. Mercier, F. Le Derf, M. Sallé, J. Org. Chem. 70, 6254 (2005)

[6] J. Lyskawa, D. Canevet, M. Allain, M. Sallé, Tetrahedron. Lett. 51, 5868 (2010)

[7] M.J. Blesa, B.T. Zhao, M. Allain, F. Le Derf, M. Sallé, Chem. Eur. J. 12, 1906 (2006)

[8] J. Lyskawa, M. Sallé, J.Y. Balandier, F. Le Derf, E. Levillain, M. Allain, P. Viel, S. Palacin, Chem. Commun. 2233 (2006)

[9] B.T. Zhao, M.J. Blesa, F. Le Derf, D. Canevet, C. Benhaoua, M. Mazari, M. Allain, M. Sallé, Tetrahedron 63, 10768 (2007)

[10] M.H. Düker, R. Gómez, C.M.L. Vande Velde, V.A. Azov, Tetrahedron Lett. 52, 2881 (2011)

[11] M.H. Lee, Q.Y. Cao, S.K. Kim, J.L. Sessler, J.S. Kim, J. Org. Chem. 76, 870 (2011)

[12] B.T. Zhao, W.B. Guo, P.Z. Hu, Heterocycles 81, 1661 (2010)

[13] B.T. Zhao, Z. Zhou, Z.N. Yan, E. Belhadj, F. Le Derf, M. Sallé, Tetrahedron Lett. 51, 5815 (2010)

[14] M. Frei, F. Diederich, R. Tremont, T. Rodriguez, L Echegoyen, Helv. Chim. Acta 89, 2040 (2006)

[15] G.M. Sheldrick, SHELXS-97, Program for the Solution of Crystal Structures (University of Göttingen, Germany, 1997)

[16] G.M. Sheldrick, SHELXL-97 Program for the Refinement of Crystal Structures (University of Göttingen, Germany, 1997)

[17] D.E. John, A.S. Batsanov, M.R. Bryce, J.A.K. Howard, Synthesis 824 (2000)

[18] N. Svenstrup, K.M. Rasmussen, T.K. Hansen, J. Becher, Synthesis 809 (1994)

[19] J. Lau, J. Becher, Synthesis 1015 (1997)

[20] I. Bitter, A. Grün, G. Toth, B. Balázs, L. Tõke, Tetrahedron 53, 9799 (1997)

[21] N. L. Allinger, X. Zhou, J. Bergsma, J. Mol. Struct. (THEOCHEM) 312, 69 (1994)

[22] N. Iki, S. Ogawa, T. Matsue, S. Miyano, J. Electroanal. Chem. 610, 90 (2007)

[23] E. Isomura, K.I. Tokuyama, T. Nishinaga, M. Iyoda, Tetrahedron Lett. 48, 5895 (2007)

[24] V.A. Azov, R. Gómez, J. Stelten, Tetrahedron 64, 1909 (2008)