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Electroactive C_2 Symmetry Receptors Based on the Biphenyl Scaffold and Tetrathiafulvalene Units

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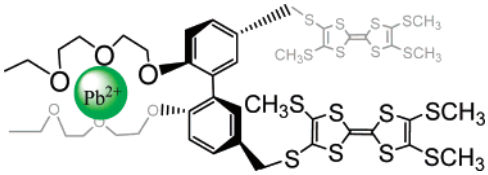
Received July 12, 2006



The synthesis of a family of biphenyl-tetrathiafulvalene (TTF) derivatives incorporating a binding site has been carried out in good to moderate yields through functionalization of the biphenyl scaffold. X-ray structure of one derivative (compound **3**) of the series is provided and shows a dihedral angle of 74° around the central Ar−Ar bond of the biphenyl unit in a *cisoid* conformation. ^{1}H NMR and cyclic-voltammetry studies demonstrate the critical importance of the nature of the substitution on the conformational rigidity and on the electrochemical behavior of the resulting biphenyl-TTF assemblies. This feature is underlined by an original electrochemical recognition process upon binding of Pb^{2+}, correlated to conformational changes occurring upon metal cation complexation.

Introduction

Due to the ability of the biphenyl unit in transmitting conformational information,[1] considerable interest has been developed around this structure which is often compared to the 1,1′-binaphthalene-2,2′-diol (BINOL) unit. Indeed, among other applications, biphenyl 2,2′-disubstituted derivatives have been used as ligands in catalysis,[2] as synthetic ionophores in the chemistry of biologically active compounds,[3] and in disaccharides recognition.[4] In particular, much progress has been made in the study of conformationally flexible biphenyls (*tropos*) in their application to stoichiometric and catalytic asymmetric reactions.[5] This reflects the importance of the biphenyl unit in stereochemical control and justifies the efforts devoted to the designing of new chiral biphenyls, more available than the configurationally stable *ortho* tetrasubstituted biphenyls. Moreover, the conformational flexibility of the biphenyl allows accommodation of a diversity of functional groups at the 2 and

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10.1021/jo061446m CCC: $33.50
Published on Web 10/28/2006

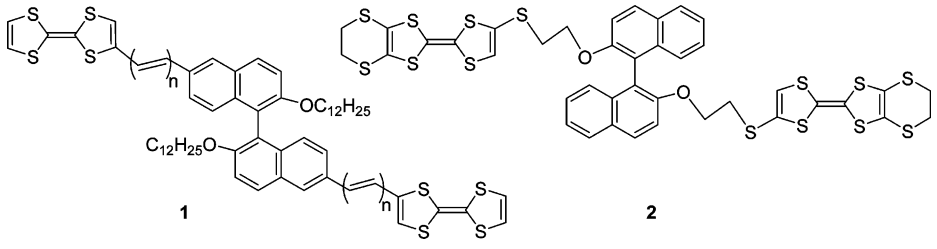

FIGURE 1. BINOL-TTF derivatives **1**[12] and **2**.[13]

2′ positions by rotation round the C1−C1′ axis without significant increase in torsional strain.

The biphenyl unit has also been extensively used in material science,[6] but, a part from some examples of biphenyl-doped chiral smectic liquid crystals,[6d,e] generally it works as a simple spacer or a linker, without taking benefit of the conformational peculiarities of this system.

The solid-state electroconducting and magnetic properties of the tetrathiafuvalene (TTF)-based materials are well established.[7] Due to its unique electrochemical properties (reversible oxidation at low potentials, to stable $TTF^{\bullet+}$ and TTF^{2+} states), the tetrathiafulvalene moiety has also appeared in recent years as an efficient redox probe in a great variety of supramolecular systems,[8] and we have been engaged in the designing of various redox-responsive receptors involving this redox unit associated to different binding sites.[9]

Examples of biphenyl-tetrathiafulvalene assemblies have been described by J. Becher et al.[10] or very recently by T. Mori et al.[11] Nevertheless none of the described products exploit the conformational features of the biphenyl scaffold. Recently N. Martín's group in Madrid reported an interesting example of BINOL linked through an *E* double bond to two tetrathiafulvalene (TTF) units (compound **1**, Figure 1).[12] It is the first example of a chiral C_2 symmetry tetrathiafulvalene dimer, designed to reach enhanced dimensionality in the corresponding materials.

The growing interest in such systems has been also very recently nicely illustrated by Zhang and Zhu who attached TTF units at the 2,2′ and 6,6′ positions of enantiopure BINOL, the latter used as a chiral scaffold (compound **2**, Figure 1).[13] The authors studied an original modulation of the circular dichroism spectrum of such assemblies, monitored by the reversible oxidation of TTF units.

We thought that 2,2′-*O*,*O*-dialkylated biphenyls substituted at the 5 and 5′ positions with TTF units were suitable candidates to study inter-TTF interactions by tuning of the biphenyl dihedral angle. Such control of interactions between redox units allows designing of original electroactive receptors whose working mode involves a transmission of a conformational recognition process to an electrochemical signal. A very recent example of such conformational control has been described with a TTF-calixarene assembly.[14] As far as we know, no assemblies involving TTF units and the biphenyl platform have been designed in this purpose, although the tuning of dihedral angle in flexible ortho−ortho′-biphenyls influenced by substituents

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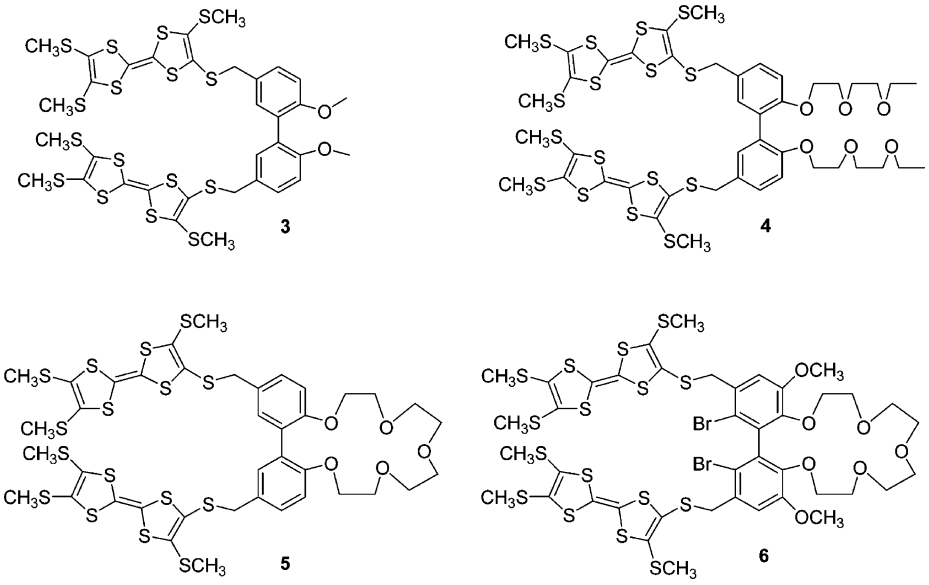
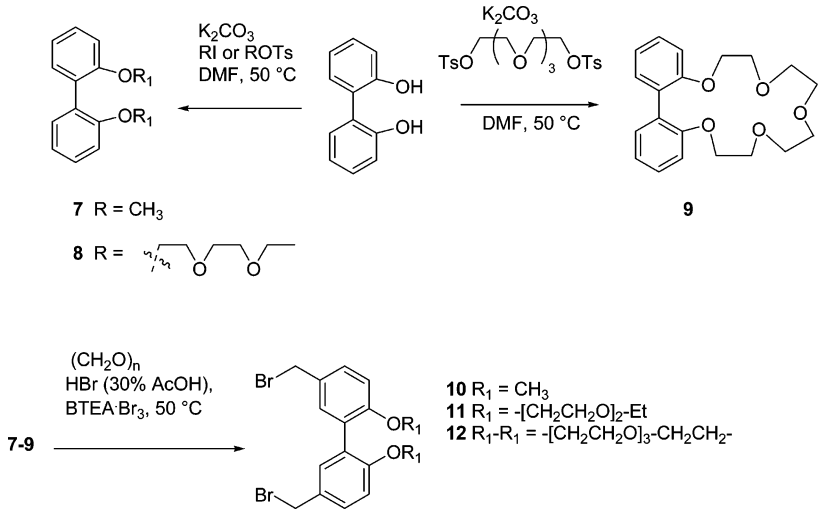


FIGURE 2. Target biphenyl-TTF structures.

SCHEME 1



at the 5,5′ positions has many examples in literature.[15] According to the nature and the size of the groups on the 2,2′ positions of the biphenyl scaffold,[16] we anticipated different electrochemical responses of the electroactive TTF units bonded at the 5,5′ positions. In particular, this effect could be amplified with biphenyl-TTF assemblies bearing a coordinating part on the 2,2′ positions and by exploring the consequence of the metal binding on the electrochemical response of the TTF unit.

Here we report on the synthesis, characterization, and electrochemical study of new biphenyls **3**−**6** bearing OR groups at the 2 and 2′ positions and two electron-donor tetrathiafulvalene units at the 5 and 5′ positions (Figure 2). X-ray structure of biphenyl-TTF assembly **3** is provided. The binding properties of these ligands toward metal cations is studied by ^{1}H NMR, as well as the effect of metal cation complexation on the electrochemical behavior of these assemblies.

Results and Discussion

Synthesis. The access to target compounds **3**−**6** involves the preparation of a series of 5,5′-bis(bromomethyl) biphenyl derivatives **10**−**12** (Scheme 1). We started the synthesis of the precursors **7**−**9** from commercially available 2,2′-biphenol. We were able to improve yield of biphenyl **9** by changing base and solvent compared to the described procedure.[17] Although compound **10** has already been described,[18] we used a more straightforward procedure[19] which we also applied to biphenyl derivatives **11** and **12,** which involved the bromomethylation reaction at the 5,5′ positions of biphenyl 2,2′-*O*,*O*′-derivatives using paraformaldehyde and a 30% HBr solution of AcOH, in

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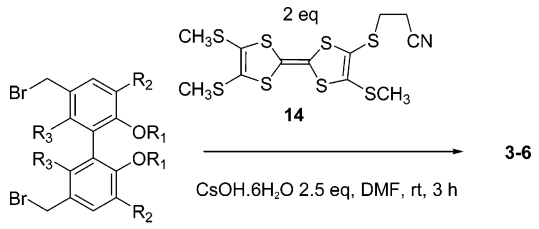
SCHEME 2



10-13

10 $R_1 = CH_3$, $R_2 = H$, $R_3 = H$
11 $R_1 = -[CH_2CH_2O]_2$-Et, $R_2 = H$, $R_3 = H$
12 R_1-$R_1 = -[CH_2CH_2O]_3$-CH_2CH_2-, $R_2 = H$, $R_3 = H$
13 R_1-$R_1 = -[CH_2CH_2O]_3$-CH_2CH_2-, $R_2 = OCH_3$, $R_3 = Br$

the presence of benzyl triethyl ammonium tribromide (BTEA·Br_3), at 50 °C.

Biphenyls **10**−**12** are conformationally flexible because of the free rotation which occurs around the single bond between aromatic rings. In order to prepare a conformationally stable biphenyl we also synthesized biphenyl derivative **13**[20] (Scheme 2) starting from *creosol* (2-methoxy-4-methyl-phenol). Biphenyl **13** is configurationally stable, and thus two enantiomers can be isolated at room temperature.

When biphenyl **10**−**13** were treated with 2 equiv of 2-(2-cyanoethylsulfanyl)-3,6,7-*tris*(methylsulfanyl)tetrathiafulvalene **14**[21] in the presence of 2.5 equiv of CsOH·$6H_2O$ in DMF, biphenyl-TTFs **3**−**6** were obtained, respectively. The reaction reached completeness in 3 h for compounds **3**−**5** which are obtained in good yields (>72%) whereas for biphenyl **13**, a longer time was required and the yield in derivative **6** did not exceed 29%. All compounds prepared are solid, air stable, and were easily separated and purified by washing the precipitate with appropriate solvents or by flash-chromatography using the appropriate solvent mixture. The assignment of the ^{1}H NMR signals was simplified in virtue of the C_2-symmetry of all compounds.

^{1}H NMR Characterization of Biphenyls 3−6. No significant differences are observed between chemical shifts of the aromatic protons (biphenyl part) of **3**−**6** (see Supporting Information) relative to those of the corresponding starting biphenyls **10**−**13**. Thus, an eventual steric or electronic effect induced by TTF units on the aromatic protons can be ruled out.

On the contrary, benzylic protons of crown-ether fused biphenyls **5** and **6** are significantly affected related to their precursors **12** and **13**, respectively, by the introduction of two TTF units. This deviation turned out to be very informative in relation with the conformation adopted by these biphenyl-TTF assemblies. Compounds **5** and **6** possess the same crown-ether fragment fused on the 2,2 positions of the biphenyl framework, as well as two TTF units at the 5,5′ positions. They essentially differ by the fact that **6** (as well as precursor **13**) is configurationally stable (2,2′,6,6′-tetrasubstituted biphenyl), whereas compound **5** (as well as precursor **12**) should be conformationally flexible. In fact, an AB system, corresponding to diastereotopic methylene protons (benzylic position), is evidenced in biphenyl **6**, as expected for a configurationally stable biphenyl (J = 13.6 Hz), as well as in **13** (J = 10.0 Hz). The increase of J value in **6** compared to **13** can be attributed to the presence of the two TTF units which induce a modification in the biphenyl conformation (dihedral angle). Most importantly, the presence of a significant AB pattern (J = 12.7 Hz) in biphenyl **5** suggests a rigidity in the system. Although biphenyl **5** is not *atropos*, the constant coupling value indicates that a conformational stability is gained at the biphenyl scaffold at least under the experimental NMR conditions. Moreover, such AB pattern is not observed in the corresponding precursor, biphenyl **12**, where a singlet is observed for benzylic protons, in accordance with a conformationally flexible (*tropos*) biphenyl and confirming that TTF units at the 5,5′-positions provide rigidity. In addition, it is interesting to note that no AB pattern is observed for **3** and **4** for which two TTF units are present but no crown-ether fragment fused on the 2,2′ positions of the biphenyl framework is present. Therefore, considering these data, it appears that both structural requirements are needed to generate a stable conformation of the biphenyl platform, i.e., a fused-crown part at the 2,2′ positions and two TTF units at the 5,5′ positions, and that these elements, considered individually, are not sufficient to promote conformational stability by their own.

X-ray Structure of Compound 3. We could obtain single crystals from slow diffusion of pentane in a dichloromethanic solution of **3**, and the corresponding X-ray structure was solved (Figure 3), even though the small size of the crystals (0.35 × 0.08 × 0.03 mm^3) precludes a high quality resolution. A critical value for biphenyl derivatives lies on the dihedral angle around the central C−C bond. The dihedral angle between both phenyl rings is 74° in compound **3**. That means that the phenyl units are in a *cisoid* conformation (the two TTF units on the one hand, and the two methoxy groups on the other hand, are located on the same side of the biphenyl scaffold) and that this conformation is comparable to other examples of 2,2′-dimethoxy substituted biphenyl derivatives.[22,23] Both TTF mean planes are roughly defined in the plane of the aromatic ring on which they are grafted. As a consequence, the two TTF skeletons are approximately arranged orthogonally in the crystal. No significant intermolecular interactions could be observed in this system.

Electrochemical Study (Cyclic Voltammetry). The electrochemical behavior of biphenyl-TTF systems **3**−**6** was studied by cyclic voltammetry in a 1:1 mixture of methylene chloride and acetonitrile (Bu_4NPF_6 (0.1 mol L^{-1})). As expected, two redox processes characteristic of the TTF moiety are observed at similar potentials in all cases (ca.: E_1^{ox} = 0.50 V, E_2^{ox} = 0.85 V vs Ag/AgCl). Nevertheless, a noticeable difference is observed between the 2,2′-disubstituted biphenyl derivatives **3**−**5** on the one hand, and the 2,2′,6,6′-tetrasubstituted **6** on the other hand. For the former compounds, the first redox wave appears broader than the second redox system (Figure 4a). At E_1^{ox}, this behavior is assigned to oxidized TTF-dimers where TTF units are interacting, leading therefore to a broadening of the first redox wave.[14] On the contrary, the second redox process (E_2^{ox}), corresponding to the formation of a tetracationic species, is thinner in accordance with independent TTF^{2+} units, which can be explained by repulsive electrostatic interactions between both dicationic species. Interestingly, the behavior is quite different for compound **6**. Both redox waves appears very similar (Figure 4b), which means there is no inter-TTF interac-

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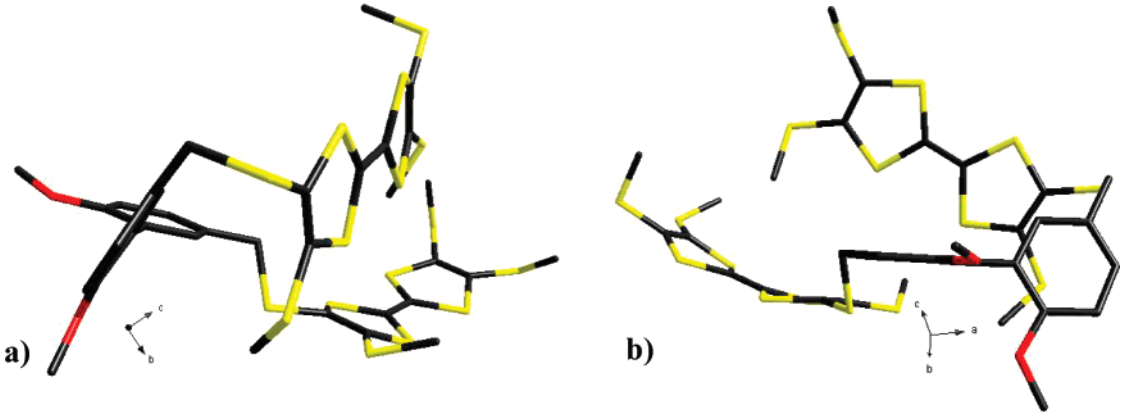

FIGURE 3. X-ray crystal structure of compound **3**.

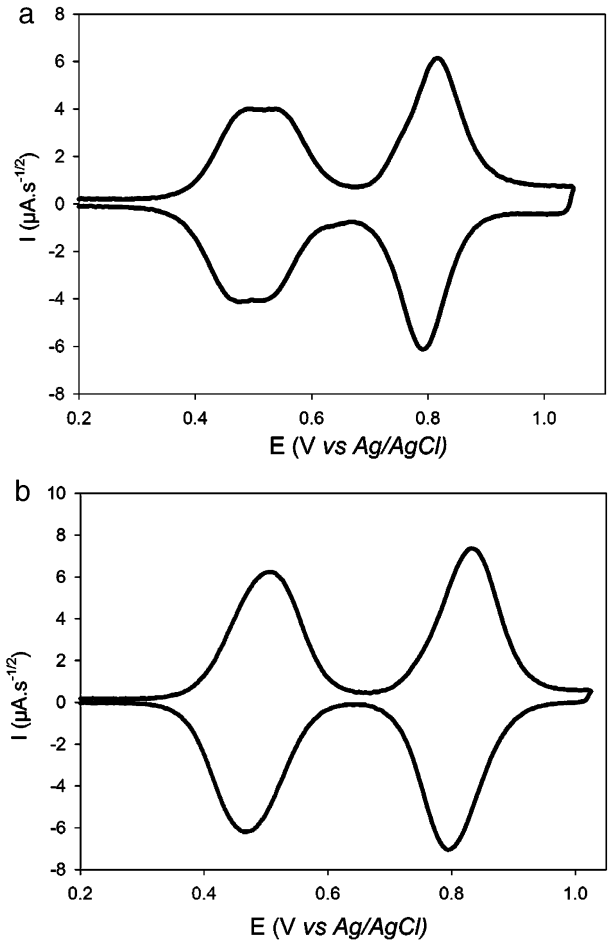

FIGURE 4. Deconvoluted voltammogram; compounds **3** (a) and **6** (b) (10^{-3} mol L^{-1}); CH_2Cl_2/CH_3CN (1/1); Bu_4NPF_6 (0.1 mol L^{-1}); 100 mV/s; Pt working electrode, diameter 1 mm; V vs Ag/AgCl.

tions at E_1^{ox} in this case. Such result was expected since the biphenyl-TTF assembly **6** has bulky substituents and it is configurationally stable, which precludes TTF units to be in close contact, at any redox states. This observation illustrates how the electrochemical behavior of redox-active biphenyl assemblies can be monitored by the degree of rotation around the biphenyl axis.

We have exploited this observation in studying the metal binding effect on the electrochemical behavior of compounds

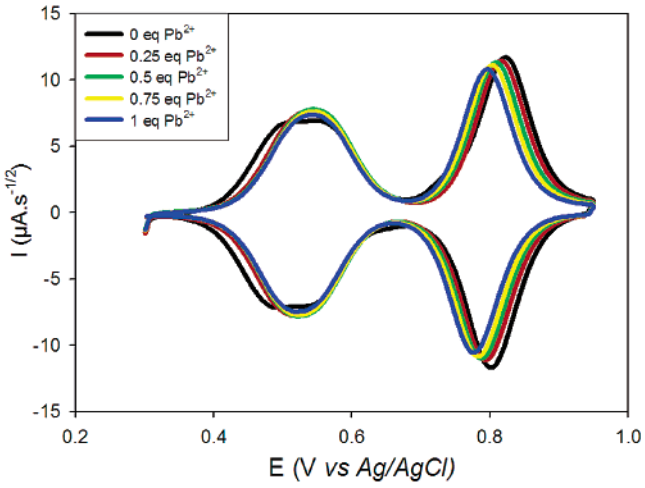

FIGURE 5. Deconvoluted voltammogram of compound **4** (10^{-3} mol L^{-1}) in the presence of increasing amounts of Pb^{2+} ($Pb(ClO_4)_2$); CH_2Cl_2/CH_3CN (1/1); Bu_4NPF_6 (0.1 mol L^{-1}); 100 mV/s; Pt working electrode, diameter 1 mm; V vs Ag/AgCl.

4−**6**, possessing a binding site. By introducing Li^+, Na^+, or K^+ (TfO^-) no noticeable effect was observed on the CV response of crown-derivatives **5** and **6**. Such behavior seems to be contrary to observations made recently in the literature with the parent compound **9**, presenting a good affinity for Na^+ (1:1 complex). In this case, complexation is allowed by the dynamic character of the dihedral angle in the sodium complex which varying around 60°, allows the metal cation to be accommodated in the crown chain.[17] Such difference between compounds **5** and **9** constitutes an additional argument to support a higher rigidity in **5** promoted by the introduction of two TTF units, leading to a lower ability for Na^+ binding. Interestingly, a striking difference is observed for the more flexible podand-derivative **4**. In this case, introduction of Pb^{2+} leads to a change in the shape of the voltamogram (Figure 5). Binding of Pb^{2+} could be characterized by several observations. Upon introduction of lead(II), the first redox wave (E_1^{ox}) appears thinner which, by analogy with the above-mentioned electrochemical behavior of the configurationally stable compound **6**, is assigned to a progressive disappearing of inter-TTF interactions. Therefore, the rigidity which is induced by Pb^{2+} coordination precludes any interactions to occur between both TTF units, a conformational phenomenon that we could also detect recently

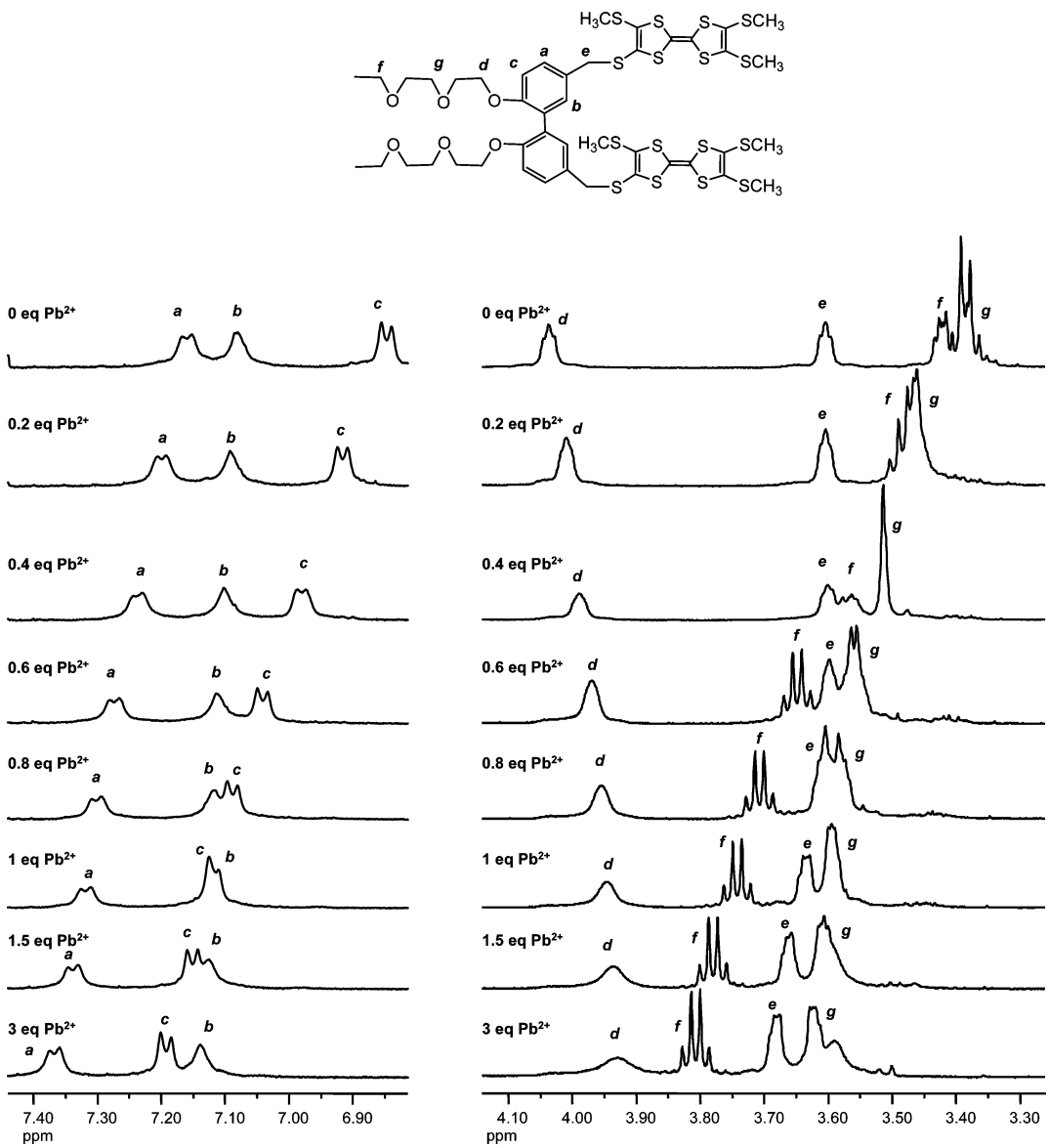

FIGURE 6. ^{1}H NMR spectra for **4** (0.014 mol L^{-1} in CD_3Cl/CD_3CN) with increasing amounts of Pb^{2+} ($Pb(ClO_4)_2$).

in a calixarene-TTF assembly.[14] Such conformational reorganization is presumably also responsible of the slight decrease observed for E_2^{ox}. Interestingly, no more evolution of the shape of the CV is observed for more than 1 equiv of Pb^{2+} added, which gives an indication about a 1:1 stoichiometry of the complex. Moreover, we verified that the CV change can be attributed to the binding of Pb^{2+} in receptor **4**, since no deviation was observed for the CV of biphenyl-TTF derivative **3**, devoid of any binding unit, upon introduction of $Pb(ClO_4)_2$. Finally, no CV change was observed in receptor **4** when it was in presence of other cations (Li^+, K^+, Ba^{2+}). This fact indicates either no complexation of these cations with **4** or that an eventual binding is not translated in an electrochemical signal.

The electrochemical recognition process as observed with biphenyl-TTF **4** in presence of Pb^{2+} is therefore different from the usual case of redox-responsive ligands, for which the bound metal cation exerts a direct electrostatic effect on the redox-probe spatially close to the binding site, leading to a shift of the redox potentials.[9b,c] In the present case, the metal binding is accompanied by a change in conformation in the assembly, relayed by the biphenyl scaffold to the redox units and illustrates how the modulation of the rotation angle in a biphenyl unit can induce a specific electrochemical response.

^{1}H NMR Titration Studies. Considering the above-mentioned electrochemical behavior of compound **4** in presence of Pb^{2+}, we also studied the binding ability by ^{1}H NMR titration. Aliquots of lead(II) perchlorate in acetonitrile-d_3 were added to a solution of **4** in a $CDCl_3/CD_3CN$ (1/1) mixture. A progressive lower field shift of several signals of **4** was observed, in accordance with a fast equilibrium process on the NMR time scale (Figure 6). As expected, the signals which are the most affected upon addition of Pb^{2+} are those corresponding to the polyethylene chain (*d*, *f*, *g*), where the metal complexation takes place. In addition, in the aromatic region, the H3, H3′ protons (signal *c*) located at the ortho positions of the polyether chain are also significantly affected. Plotting the variation of chemical shifts vs the amount of Pb^{2+} introduced generates a plateau for ca. 1 equiv of metal cation (Figure 7), confirming a 1:1 stoichiometry for the complex. From these data, and using the EQNMR program,[24] a $K°$ value of $10^{3.42 \pm 0.21}$ is found from

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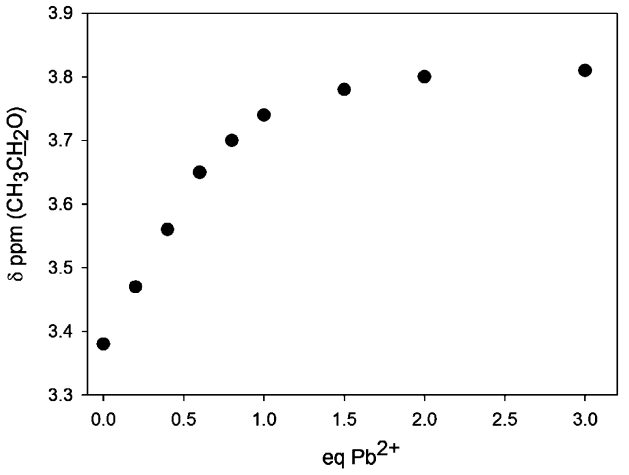

FIGURE 7. ^{1}H NMR titration curve for **4** (0.014 mol L^{-1} in $CDCl_3$/CD_3CN) (*f* signal) with increasing amounts of Pb^{2+} ($Pb(ClO_4)_2$).

^{1}H NMR (see Figure 6) ($CDCl_3$, CD_3CN, 20 °C). Noteworthy, no deviation of the ^{1}H NMR signals was observed by introducing K^+ (triflate) on **4** under similar conditions, which actually confirms a preference of this binding site for lead(II) over alkaline cations.[9c]

Conclusion

A series of biphenyl-TTF derivatives bearing a binding site has been synthesized. Synergic steric influence of TTF substituents and crown-ether chain bonded to the biphenyl scaffold has been observed in conformationally flexible biphenyls by NMR experiments. This highlights how substituents at the *meta*−*meta*′ and *ortho*−*ortho*′ positions of the biphenyl are crucial in the tuning of dihedral angle and therefore in the preparation of TTF-biphenyl assemblies with electrochemical recognition behavior. Our study confirms that it is possible to reach TTF-atropoisomeric assemblies, starting from *tropos* biphenyls[5j,m] instead of conformationally stable biphenyls (atropos) or binaphthyls. In fact electrochemical behavior of **3**−**6** appears to be strongly dependent on the conformational flexibility of the molecular assembly. In particular, the Pb^{+2} binding ability of one member of the series, compound **4**, could be electrochemically (CV) addressed through conformational modifications relayed by the biphenyl scaffold. Such architectures constitute a suitable model to study long-distance conformational effects monitored electrochemically. Extension of this work to design new responsive receptors is under investigation.

Experimental Section

X-ray Structural Data. Crystal data for **3**: $C_{34}H_{34}O_2S_{16}$, M_r = 987.57, monoclinic, space group $P2_1/c$, a = 11.3922(9) Å, b = 7.8682(5) Å, c = 48.276(7) Å, β = 95.37(1)°, V = 4308.3(8) Å,^{3} Z = 4, ρcalc = 1.523 gcm^{-3}, μ (Mo Kα) = 0.835 mm^{-1}, F(000) = 2040, crystal dimension = 0.35 × 0.08 × 0.03 mm^3, θmin = 1.80°, θmax = 25.84°, 15429 reflections collected, 4975 unique (R_{int} = 0.122), restraints/parameters = 0/209, $R1$ = 0.0913 and $wR2$ = 0.2047 using 1383 reflections with $I > 2\sigma(I)$, $R1$ = 0.2591 and $wR2$ = 0.2572 using all data, GOF = 0.783, −0.844 < $\Delta\rho$ < 0.900 e Å^{-3}.

Preparation of Compounds 3−6, General Procedure. A solution of $CsOH{\cdot}6H_2O$ (0.250 mmol) in dry MeOH (2 mL) was added, under N_2, to a solution of the 2-(2-cyanoethylsulfanyl)-3,6,7-*tris*(methylsulfanyltetrathiafulvalene (0.200 mmol) in dry DMF (10 mL) for 15 min. The resulting solution was stirred for 30 min at room temperature. A solution of the biphenyl (0.100 mmol) in dry DMF (5 mL) was added. This resulting solution was stirred for 3 h at room temperature and then concentrated in vacuum.

Compound 3. A precipitate is formed, and subsequently, it was filtrated and washed. The solid was dissolved in dichloromethane and washed with water. Then, it was dried with $MgSO_4$ and evaporated. Finally, it precipited and was washed with cold acetone. An orange solid **3** was obtained in 72% of yield. Mp: 158 °C. ^{1}H NMR ($CDCl_3$): 7.27 (d, J_{ortho}= 8.5 Hz, 2H), 7.17 (bs, 2H), 6.89 (d, J_{ortho}= 8.5 Hz, 2H), 3.99 (s, 4H), 3.73 (s, 6H), 2.42 (s, 6H), 2.41 (s, 6H), 2.27 (s, 6H). ^{13}C NMR ($CDCl_3$): 156.6, 132.1, 129.4, 128.4, 127.8, 127.3, 111.1, 55.9, 40.2, 31.0, 19.2. HR-ESI-MS (*m*/*z*): $C_{34}H_{34}O_2S_{16}$ Calcd: 985.8090. Found: 985.8129.

Compound 4. Water was added, and the solution was extracted with ether. The organic layer was evaporated to give a yellow solid that was purified by flash chromatography (ethyl acetate/petroleum ether 1:1) to get the target product **4** in 75% yield. Mp: 82 °C. ^{1}H NMR ($CDCl_3$): 7.15 (broad d, J_{ortho} = 9.0 Hz, 2H), 7.13 (broad s, 2H), 6.80 (d, J_{ortho} = 9.0 Hz, 2H), 4.00 (t, J = 8.5 Hz, 4H), 3.96 (bs, 4H), 3.62 (t, J = 8.5 Hz, 4H), 3.39−3.45 (series of m, 12H), 2.48 (bs, 18H), 1.12 (t, J = 9.0 Hz, 6H). ^{13}C NMR ($CDCl_3$): 155.9, 132.4, 129.3, 128.5, 128.1, 112.3, 70.9, 69.9, 68.5,69.7, 66.7, 19.3, 15.3. ^{1}H NMR (C_6D_6): 7.31 (d, 2H, J_{meta} = 2.4 Hz, 2H), 7.09 (dd, J_{meta} = 2.4 Hz, J_{ortho} = 8.8 Hz, 2H), 6.58 (d, J_{ortho} = 8.8 Hz, 2H), 3.83 (s, 4H), 3.79 (t, J = 4.8 Hz, 4H), 3.46 (t, J = 4.8 Hz, 4H), 4.12−3.28 (series of m, 12H), 1.89 (s, 6H), 1.87 (s, 6H), 1.86 (s, 6H), 1.10 (t, J = 7.2 Hz, 6H). HR-ESI-MS (*m*/*z*): $C_{44}H_{54}O_6S_{16}Na$ Calcd: 1212.9350. Found: 1212.9399 $(M + Na)^+$.

Compound 5. A precipitate is formed, and subsequently, it was filtrated and washed. The solid was redisolved in dichloromethane and washed with water. Then, it was dried with $MgSO_4$ and evaporated. Finally, it precipitated and was washed with cold acetone. A yellow solid **5** was obtained in 81% of yield. Mp: 161 °C. ^{1}H NMR ($CDCl_3$): 7.24 (dd, J_{meta} = 2.0 Hz, J_{ortho} = 8.5 Hz, 2H), 7.13 (d, J_{meta} = 2.0 Hz, 2H), 6.88 (d, J_{ortho} = 8.5 Hz, 2H), 4.18 (m, 2H), 3.99 (AB, 4H, J = 12.7 Hz), 3.96 (m, 2H), 3.80 (m, 2H), 3.73−3.68 (series of m, 4H), 3.61−3.56 (series of m, 6H), 2.42 (s, 6H), 2.41 (s, 6H), 2.27 (s, 6H). ^{13}C NMR ($CDCl_3$): 155.8, 131.9, 129.0, 128.2, 128.1, 127.3, 127.0, 124.7, 111.7, 110.8, 109.9, 70.8, 70.6, 69.4, 67.7, 39.9, 19.0, 18.9.

MS (Maldi-tof): *m*/*z* 1116.19. HR-ESI-MS (*m*/*z*): $C_{40}H_{44}O_5S_{16}Na$ Calcd: 1138.8880. Found: 1138.8925 $(M + Na)^+$.

Compound 6. The crude was evaporated. The solid residue was dissolved in dichloromethane, washed with water, and then dried with $MgSO_4$. After removing the dichloromethane, a silica gel column was carried out (a. DCM; b. DCM:MeOH 10:0.17, c. DCM, MeOH 10:0.20) to get the target product **6** in 29% of yield. Mp: 65 °C. ^{1}H NMR ($CDCl_3$): 6.91 (s, 2H), 4.23 (m, 2H), 4.11 (AB, 4H, J = 13.6 Hz), 3.96 (m, 2H), 3.84 (s, 6H), 3.69 (m, 2H), 3.65−3.56 (series of m, 4H), 3.51−3.42 (series of m, 6H), 2.44 (s, 6H), 2.42 (s, 6H), 2.31 (s, 6H). ^{13}C NMR ($CDCl_3$): 151.4, 146.2, 134.4, 131.1, 131.5, 127.4, 127.2, 123.5, 116.8, 114.1, 111.6, 110.8, 71.6, 70.9, 70.1, 69.7, 55.9, 41.6, 19.3, 19.2. MS (Maldi-tof): *m*/*z* 1331.57. HR-ESI-MS (*m*/*z*): $C_{42}H_{46}Br_2O_7S_{16}$ Calcd: 1331.7142. Found: 1331.7179.

Compound 8. A solution of KOH (0.74 g, 13.2 mmol) in H_2O (8 mL) was added at 0 °C to a solution of 2,2′-biphenol (1.1 g, 6 mmol) in THF (50 mL). The resulting solution was stirred for 30 min at room temperature. A solution of diethylenglicol monoethylether *O*-tosylate (3.8 g, 13.2 mmol) in THF (50 mL) was added. This resulting solution was stirred for 12 h at 60 °C and then concentrated in vacuum. Water was added, and the solution was extracted with ether. The organic layer was evaporated to give a yellow oil that was purified by flash chromatography (petroleum ether/dichloromethane: 1/1) to get the target product **8** in 81% yield. ^{1}H NMR ($CDCl_3$): 7.29−7.24 (series of m, 4H), 6.98 (dd, J_{meta} = 1.0 Hz, J_{ortho} = 7.6 Hz, 2H), 6.93 (dd, J_{meta} = 0.9 Hz, J_{orhto} = 8.1 Hz, 2H), 4.08 (t, J = 5.6 Hz, 4H), 3.69 (t, J = 5.2 Hz, 4H), 3.50−

3.43 (series of m, 12H), 1.18 (t, J = 6.8 Hz, 6H). ^{13}C NMR ($CDCl_3$): 156.6, 131.9, 128.6, 128.5, 120.7, 112.6, 71.2, 70.1, 69.9, 68.8, 66.80, 15.4.

Compound 9. Into a tree round-bottom flask containing a suspension of K_2CO_3 (5.4 g, 39.0 mmol) in dry DMF (200 mL), a solution of 2,2′ biphenol (0.73 g, 3.90 mmol) in dry DMF (60 mL) and a solution of tetraethylene glycol ditosylate (2.00 g, 3.90 mmol) in dry DMF (60 mL) were added simultaneously and very slowly under N_2. The reaction mixture was stirred at 50 °C for 1 day. Then water was added and the organic phase extracted with ethyl ether (50 mL × 3), dried over Na_2SO_4, and evaporated to dryness. A colorless oil was recovered that was purified by flash chromatography using a 2:1 mixture of petroleum ether:ethyl acetate as eluent to give **9** as solid (0.520 g, yield 39%). ^{1}H NMR ($CDCl_3$): 7.30 (tdd, J_{meta} = 1.7 Hz, J_{ortho} = 8.0 Hz, 2H), 7.15 (dd, J_{meta} = 1.7 Hz, J_{ortho} = 7.4 Hz, 2H), 6.99 (tdd, J_{meta} = 1.0 Hz, J_{orhto} = 7.4 Hz, 2H), 6.99 (dd, J_{meta} = 1.0 Hz, J_{ortho} = 8 Hz, 2H), 4.22−3.54 (series of m, 16H). ^{13}C NMR ($CDCl_3$): 156.5, 131.8, 128.9, 128.3, 120.7, 113.2, 70.9, 70.6, 69.7, 68.9.

General Procedure of Bromomethylation Reaction. To a solution of 2,2′-*O*,*O*-dialkylated-biphenyl **7**-**10** (1 equiv) in acetic acid (0.77 M) was added with vigorous magnetic stirring, HBr (33% in acetic acid, 4.1 equiv), benzyltriethylammonium tribromide (0.02 equiv), and paraformaldehyde (2 equiv). The solution was stirred at 50 °C for 1 h, then water and a saturated acqueous solution of $Na_2S_2O_5$ were added to the mixture. The organic phase was extracted with dichloromethane, dried over Na_2SO_4, and evaporated to afford a colorless solid or a colorless oil.

Compound 10. The oil was purified by flash chromatography (ethyl acetate/petroleum ether: 1/1) to get compound **10** as a white solid (2.31 g, 50% yield). ^{1}H NMR ($CDCl_3$): 7.37 (dd, J_{meta} = 2.4 Hz, J_{ortho} = 8.4 Hz, 2H), 7.28 (d, J_{meta} = 2.4 Hz, 2H), 6.93 (d, J_{ortho} = 8.4 Hz, 2H), 4.53 (s, 4H), 3.78 (s, 6H). ^{13}C NMR ($CDCl_3$): 34.2, 56.0, 111.4, 127.7, 129.7, 129.8, 132.5, 157.3.

Compound 11. The oil was purified by flash chromatography (ethyl acetate/petroleum ether: 1/1) to get the target product **11** in 45% yield. ^{1}H NMR ($CDCl_3$): 7.31 (d, J_{meta} = 2.0 Hz, 2H), 7.28 (dd, J_{meta} = 2.0 Hz, J_{ortho} = 8.4 Hz, 2H), 6.88 (d, J_{ortho} = 8.4 Hz, 2H), 4.49 (s, 4H), 4.07 (t, J = 5.2 Hz, 4H), 3.69 (t, J = 5.2 Hz, 4H), 3.43−3.50 (series of m, 12H), 1.16 (t, J = 7.2 Hz, 6H). ^{13}C NMR ($CDCl_3$): 156.5, 132.8, 129.9, 129.7, 127.7, 112.6, 71.2, 70.1, 69.8, 68.7, 66.8, 34.3, 15.4.

Compound 12. The crude product was purified by flash chromatography using a 1:1 mixture of petroleum ether:ethyl acetate as eluent to give **12** as white solid (0.47 g, yield 59%). ^{1}H NMR ($CDCl_3$): 7.34 (d, J_{meta} = 2.0 Hz, 2H), 7.23 (dd, J_{meta} = 2.0 Hz, J_{ortho} = 8.4 Hz, 2H), 6.93 (d, J_{ortho} = 8.4 Hz, 2H), 4.53 (s, 4H). ^{13}C NMR ($CDCl_3$): 156.4, 131.8, 129.4, 129.1, 127.8, 112.6, 70.8, 70.6, 69.6, 68.8, 35.4.

Compound 13. The solid was purified by flash chromatography (acetone/petroleum ether: 1/2) to get the target product **13** in 44% yield. Mp: 144 °C. ^{1}H NMR ($CDCl_3$): 7.06 (s, 2H,), 4.65 (AB, J = 10.0 Hz, 4H), 4.32 (m, 2H), 3.98 (m, 2H), 3.89 (s, 6H), 3.40−3.70 (series of m, 12H). ^{13}C NMR ($CDCl_3$): 151.9, 147.0, 134.4, 132.2, 116.9, 114.1, 71.9, 70.8, 70.1, 69.8, 56.0, 35.1.

Acknowledgment. Researcher exchanges between both laboratories have been partly funded by a PAI Galileo (No. 06977VG) as well by as by the COST D31 Action which are acknowledged. M.S. thanks the Institut Universitaire de France (IUF) for its financial support. Dr. D. Rondeau (Service Commun d'Analyses Spectroscopiques) is gratefully acknowledeged for performing HRMS.

Supporting Information Available: X-ray crystallographic data (Cif files) of compound **3**. ^{1}H NMR and ^{13}C NMR spectra for compounds **3**−**6** as well as additional experimental synthetic details. This material is available free of charge via the Internet at http://pubs.acs.org.

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