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Synthesis of electrochemically responsive TTF-based molecular tweezers: evidence of tight intramolecular TTF pairing in solution

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Dedicated to Professor Fredric M. Menger on the occasion of his 70th birthday

Abstract

We report the synthesis and conformational studies of TTF-containing molecular tweezers based on a 1,2,4,5-tetramethylbenzene scaffold. In the neutral form the tweezers are expected to adopt the *closed* conformation, while, upon oxidation, the *open* conformation should be preferred due to electrostatic repulsion between the oxidized TTF moieties. Cyclic voltammetry studies demonstrate electronic pairing with formation of mixed-valence $[\mathrm{TTF}]_2^{+\bullet}$ species and opening of the tweezers upon the full oxidation of the TTF groups. Variable-temperature (VT) NMR studies evidence tight intramolecular TTF pairing at low temperature. Molecular modeling studies showed clear preference for an *open* conformation of tweezers in a fully oxidized state.

Keywords: Molecular devices; Conformational analysis; NMR; Cyclic voltammetry; Tetrathiafulvalenes; Stacking

1. Introduction

During the last several years considerable efforts have been aimed at the design and construction of molecular switches and molecular devices displaying positional displacement of molecular or supramolecular components as a result of external stimuli.[1] Numerous molecular architectures displaying rotation around a bond,[2] shuffling,[3] rotation in a catenane,[4] coiling/decoiling,[5] and other types of movements have been reported so far. External stimuli such as light, heat, pH change, complexation/decomplexation, and oxidation/reduction have been used to induce molecular displacement in these systems. Nevertheless, despite the wide variety of functional molecular architectures already developed and investigated, there are still many open possibilities to design and assemble molecular machines displaying novel modes of molecular motions. Therefore, the construction of molecular systems capable of controlled molecular-level motion has become an area of great contemporary interest and scientific growth.

Noncyclic compounds with cavities commonly called molecular tweezers, clips, or clefts[6,7] have been already successfully employed as molecular hosts for guest binding in solution as well as in solid state. Another not yet deeply exploited possibility of this type of materials is to use clip-like architectures with sufficient conformational freedom for the construction of switching structures able to perform large-scale *open*−*close* movement resembling a flapping wing motion of birds or flying insects. In a *closed* conformation the two tips of the tweezers overlay each other, whereas in an *open* conformation the tips open up opposite to each other.

The objective of this work is to design and synthesize a novel red/ox responsive tweezers-type molecular architecture capable of controllable and geometrically well-defined large-scale molecular movement.[8] For this purpose, we have chosen tetrathiafulvalene (TTF) as an appropriate building block. One of the advantages of TTF is the versatility of its chemistry,[9]

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which provides a wide range of functionalized derivatives and paves the way to its employment for the construction of various architectures, such as TTF-based chiral dimers,[10] dendrimers,[11] cyclophanes and cages,[12] and other complex structures. On the other hand, TTF is a good two-electron donor, which undergoes aromatization upon oxidation, affording thermodynamically stable radical cationic and dicationic species at relatively low oxidation potentials. This behavior has enabled the synthesis of donor–acceptor systems with promising applications: in non-linear optics, as sensors, rectifiers, or even as solar energy converters.[13] Moreover, TTF has an excellent record of application in various areas of supramolecular chemistry[9] including the construction of various types of molecular machines.[3c–e,14] All these outstanding characteristics motivated us to select TTF as the red/ox active actuator in our molecular switches.

2. Results and discussion

2.1. Molecular design

Molecular tweezers **1** (Fig. 1) were designed to contain two identical TTF moieties connected on their ends to the opposite sides of a 1,2,4,5-substituted benzene scaffold via moderately flexible eight-membered dithia rings, in a similar way to the family of molecular tweezers first designed by Fukazawa et al.[7] on the basis of the dioxa[2.2]orthocyclophane skeleton. Despite an extensive development of TTF chemistry, only a few TTF-containing rigid molecular tweezers[15] or structures preferring to adopt a tweezers-like conformation in a solid state (either neutral[16a] or oxidized[16b,c]) have been reported so far. This molecular architecture is relatively rigid having only a few low-energy conformations geometrically quite different one from another. Conformational analysis of cycloocta-1,5-diene-like ring systems[17] (eight-membered rings with two fixed torsion angles opposite to each other), similar to the dithia rings of **2**, indicates the existence of three low-energy conformations: *boat*, *chair*, and *skew* (Fig. 2). Combinations of these three conformations can lead to several possible low-energy conformations for the tweezers **1**, some of which are shown in Figure 1 to illustrate the geometrical differences between them. Only one of the conformations (*cis-boat–boat*) shows a tweezers-like arrangement of the structure, with the TTF planes positioned almost parallel at ca. 6 Å away from each other, in all others the TTF units are located remotely apart from each other with distances reaching ca. 22.5 Å between the ends of the molecular backbone. The interconversion energy between different conformations should be relatively small: previous experimental and theoretical estimations for activation energy of *boat–skew–boat* conformational introversion for cycloocta-1,5-diene-like rings vary from 1.1 to 7.5 kcal/mol,[17a] whereas for the *chair–boat* the activation energy was reported to lie within the 7.2–10.2 kcal/mol range.[17a,c]

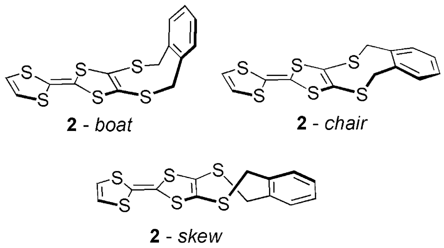


Figure 2. Three low-energy conformers of **2**.

In order to estimate the conformational preferences of the clefts **1**, structure **2** containing one eight-membered dithia ring fused with both a TTF moiety and a benzene ring has been theoretically studied as a model compound. The semi-empirical minimization of the three low-lying conformations using AM1 and PM3 methods showed very low-energy difference between the *boat*, *chair*, and *skew* conformations all lying within a narrow 2 kcal/mol energy range (Table 1), the *boat* conformation being slightly preferential to the other two.

Table 1
Relative energies (kcal/mol) of the three conformations of **2**

	PM3	AM1
Boat	0.25	1.23
Chair	0	0
Skew	1.84	0.74

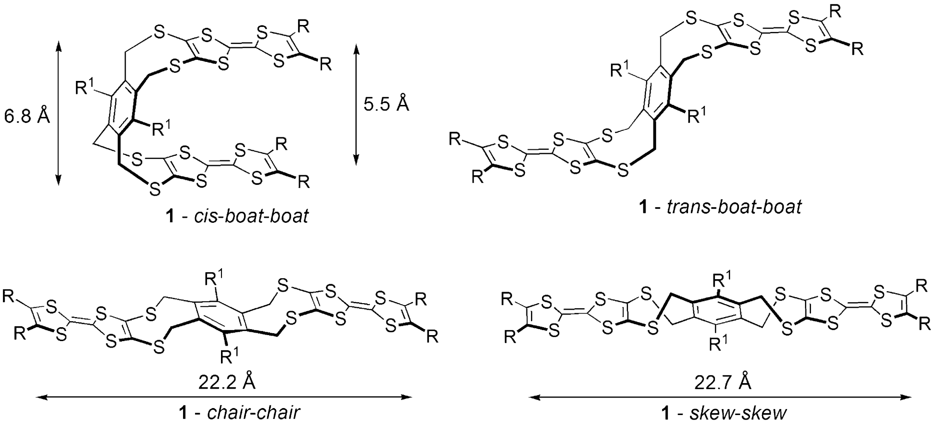


Figure 1. Selected low potential energy conformations of molecular tweezers **1** (not all possible conformations are shown). R=SAlkyl, R^1=H, OAlkyl.

Thus, if only conformational preferences of the eight-membered rings were considered, all possible combinations of *boat*, *chair*, and *skew* conformations could coexist for molecular tweezers **1**. Taking into account the relatively poor ability of ab initio computational methods, even at high-level, to predict energies of aromatic stacking interactions,[18] modeling the full structures with semi-empirical methods only provides a rough assessment of its geometry showing that all possible combinations lie within a 2 kcal/mol (AM1) or 4 kcal/mol (PM3) energy window.

2.2. Synthesis and properties

Molecular tweezers **1a–c** (Scheme 1) were prepared by the reaction of TTF dithiolates **3a′** and **3b′**, generated in situ from 2,3-bis(2-cyanoethylthio)-tetrathiafulvalenes[19] **3a** and **3b**, respectively, and tetrabromodurene derivatives **4a** and **4b**.[20,21] Preparations were performed in a similar manner to the previously reported ones.[20,22] Purification by column chromatography in dichloromethane/petroleum ether mixtures afforded pure products with 41–56% yields. Compounds were characterized by means of NMR (^{1}H and ^{13}C), MS (ESI and Hi-Res MALDI), and UV/vis spectroscopy. ^{1}H NMR did not display any splitting of the methylene protons of the eight-membered dithia ring suggesting a fast conformational equilibration at room temperature. The UV/vis spectra (CH_2Cl_2, 293 K) of compounds **1a–c** featured typical absorption pattern for tetrathio-substituted TTF derivatives[11a,22,23] with absorption bands at λ_{max} ca. 300 and 330 nm, as well as a shoulder at ca. 415 nm (Fig. 3a). All three compounds are colored solids (orange-red or dark yellow) having high (**1a**) or modest (**1b** and **1c**) solubility in common non-polar organic solvents (dichloromethane, toluene), and are easily oxidizable by air when in solution.

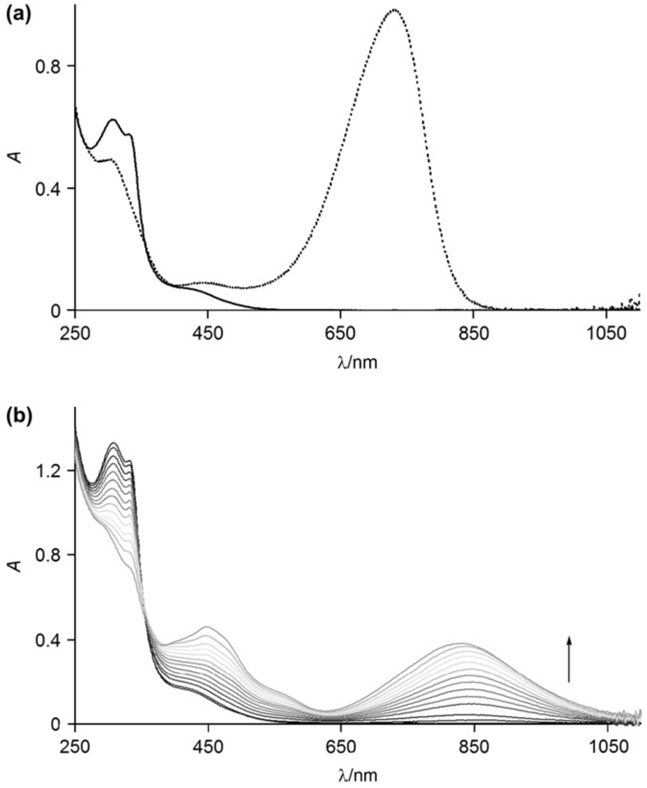
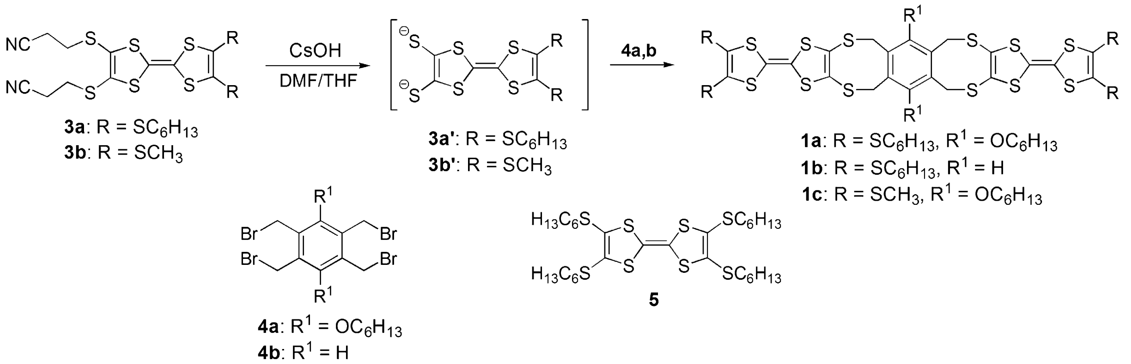


Figure 3. (a) UV/vis spectrum of **1a** (CH_2Cl_2, 2×10^{-5} M, —) and $\mathbf{1a^{4+}\cdot 4SbF_6^-}$ (CH_2Cl_2, 2×10^{-5} M, ···); (b) spectral changes observed for **1a** (CH_2Cl_2, 4×10^{-5} M) upon titration with $NOSbF_6$ up to 2 equiv.

Compound **1a** could be oxidized without decomposition by the addition of 4 equiv of $NOSbF_6$ (added as a solution in acetonitrile) in degassed stabilizer-free dichloromethane at −40 °C giving a dark-blue solution. The $\mathbf{1a^{4+}}$ tetracation (as well as the $\mathbf{5^{2+}}$ dication) was characterized by NMR (see Supplementary data, Figs. S6 and S7) and did not show traces of decomposition upon heating up to room temperature. The UV spectrum of $\mathbf{1a^{4+}\cdot 4SbF_6^-}$ at room temperature displays a strong absorption band at λ_{max} 728 nm (ε 49,000 $M^{-1}\,cm^{-1}$, 24,500 $M^{-1}\,cm^{-1}$ per each TTF unit) (Fig. 3a), similar to $\mathbf{5^{2+}\cdot 4SbF_6^-}$ with λ_{max} 738 nm (ε 22,000 $M^{-1}\,cm^{-1}$). At room temperature a dichloromethane solution of **1a** could be titrated without decomposition with up to 2 equiv of $NOSbF_6$ displaying the development of strong absorption bands with maxima located at 843 and at 445 nm (Fig. 3b). Both bands are characteristic of tetrathio-substituted $TTF^{+\bullet}$ radical cations[22,24] and similar to those of $\mathbf{5^{+\bullet}}$, with maxima located at 868 and at 455 nm, respectively.

2.3. Electrochemistry

Tweezer **1a** has been electrochemically studied to examine the influence of the TTF–TTF interaction on its redox and



Scheme 1.

conformational behavior. Thus, cyclic voltammetry (CV) measurements were carried out in dichloromethane solution and using tetrabutylammonium perchlorate as the supporting electrolyte, platinum as the working and counter electrode, and Ag/Ag$^+$ as the reference electrode. The cyclic voltammograms of **1a** show the presence of two quasi-reversible electrochemical processes on the cathodic scan, the first one splitting into two relatively well-defined waves at $E_{1/2}$=0.30 and 0.42 V, and the second one at 0.66 V (Fig. 4). Tetrakis(hexylthio)tetrathiafulvalene **5** was also electrochemically investigated as a reference for comparison, undergoing two 1e$^-$ reversible oxidation steps ($E_{1/2}$=0.34 and 0.63 V), the first leading to the TTF radical cation and the second to the TTF dication, as it is known from literature.[9] It has been reported that when two or more TTF moieties in the same molecule are sufficiently close to each other, the first oxidation to the bis(radical cation) is broadened or split into two steps[25] as in our case. This fact suggests an electronic stabilization of the first-formed radical cation by the π electrons of the neighboring TTF moiety leading to a reduction of the potential of the first 1e$^-$ oxidation step. Furthermore, the second 1e$^-$ oxidation step becomes more difficult as a result of the proximity of the first-formed radical cation, thus explaining the cathodic shift of this process (i.e., the second oxidation is more difficult due to the proximity of the firstly-formed radical cation). Therefore, we can conclude that the first two overlapping waves in the voltammograms of **1a** can be assigned to the 1e$^-$ sequential formation of **1a** mono(radical cation) and bis(radical cation), respectively. The reversible second two-electron process leading to the formation of the dication indicates that the two chromophores are at larger distance and no longer in electronic communication,[26] whereas the first two 1e$^-$ oxidations of **1a** indicate that these processes proceed when both TTF units are in close proximity to each other. Thus, *closed* conformation of the molecular tweezer **1a** is likely preferred at least in the mono-oxidized state and cyclic voltammetry gives in this way an indication of the conformational transition to an *open* conformation due to *Coulombic* repulsion between the two doubly charged TTF moieties.

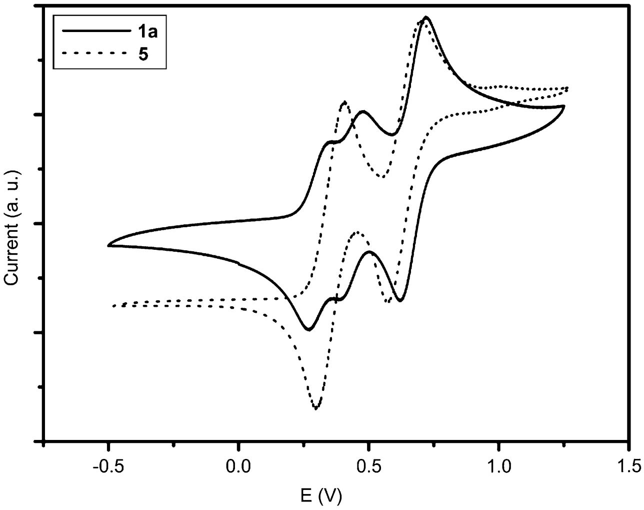


Figure 4. Comparative CV of the tweezers **1a** and tetrakis(hexylthio)tetrathiafulvalene **5** (CH_2Cl_2, 20 °C, 0.1 M Bu_4NPF_6, scan rate 200 mV/s).

2.4. Variable-temperature NMR (VT-NMR)

NMR of **1a** at room temperature (Fig. 5a) displayed a unique singlet for the $-CH_2-$ groups (H^c) located between the benzene ring and the TTF moiety, suggesting fast conformational equilibration of the two eight-membered rings at room temperature. To estimate the energy barriers for conformation interconversion of **1a**, VT-NMR experiments were conducted at low temperature in CD_2Cl_2 solution. The experiments showed that conformational switching froze on an NMR timescale at about 200 K. The resonance of the H^c methylene group at 4.34 ppm split into an AB quartet, whereas the H^f (alkylthio-methylene group) triplet at 2.74 ppm broke up into two broadened multiplets when temperature reached 203 K (Fig. 5a). The splitting of alkylthio-methylene group H^f was also confirmed by low-temperature COSY experiments (Fig. 5b), which displayed strong cross-peaks for two broadened multiplets at 2.45 and 2.78 ppm. The inequivalence of the two protons of the alkylthio-methylene group at low temperature indicates that the free rotation of the thioalkyl chain is frozen suggesting a stacking of the TTF moieties. Thus, the splitting patterns of H^c and H^f protons confirm the preferential alignment of **1a** in the *closed* tweezers-like conformation with tight contacts between the TTF flaps at low temperature. NMR spectra at low temperatures did not display the presence of any other conformations of **1a**, testifying that the *closed* conformation is the most energetically preferred one. By monitoring the signals of H^c and H^f (coalesced at 209 and 211 K, respectively) the activation free enthalpy $\Delta G^{\ddagger}$ for the conformational equilibration of **1a** was estimated as 10.1±0.5 kcal/mol using methods of dynamic NMR spectroscopy.[27] Taking into account that conformational averaging can proceed through *boat–skew–boat*[17a] conformational introversion of the eight-membered ring with the activation energy of the process lying in the range from 1.1 to 7.5 kcal/mol,[17] we can deduce that the attractive TTF–TTF interaction increases the activation free enthalpy by 2.6–9 kcal/mol. It is reasonable to assume that this raise of activation free enthalpy $\Delta G^{\ddagger}$ largely represents the magnitude of the pairing interactions between the two TTF units in CD_2Cl_2. More precise experimental and theoretical investigations of the conformational processes of the flexible structural element—eight-membered ring—are in progress now to increase the accuracy of the assessment.

Unlike as for pure **1a**, VT-NMR scans of $\mathbf{1a^{4+}\cdot 4SbF_6^-}$ in CD_2Cl_2 displayed a sharp singlet for the H^c methylene protons—an evidence for fast conformational equilibration on the NMR timescale (see Supplementary data, Fig. S8) up to 213 K.

2.5. Molecular modeling of the oxidized tweezers

To explain the conformational behavior of the oxidized tweezers $\mathbf{1^{4+}}$ (R, R^1=H) additional molecular modeling studies were performed. Despite semi-empirical optimization did

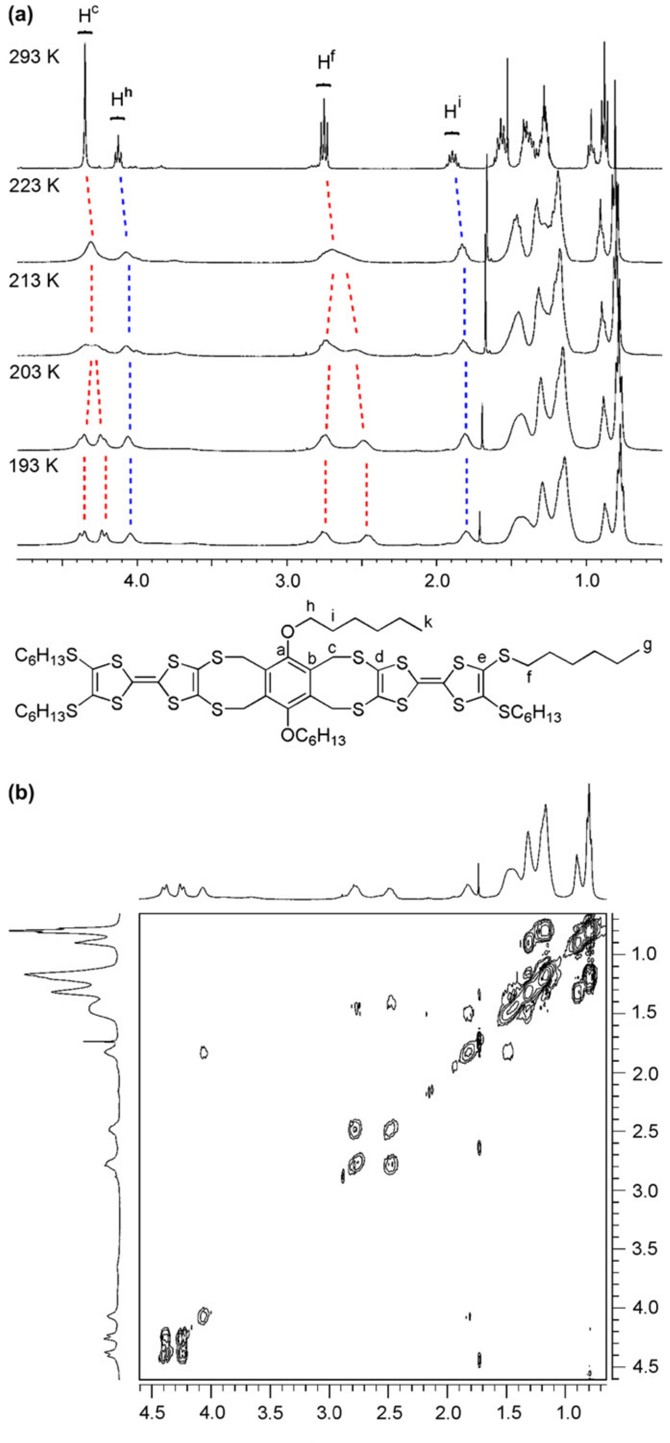
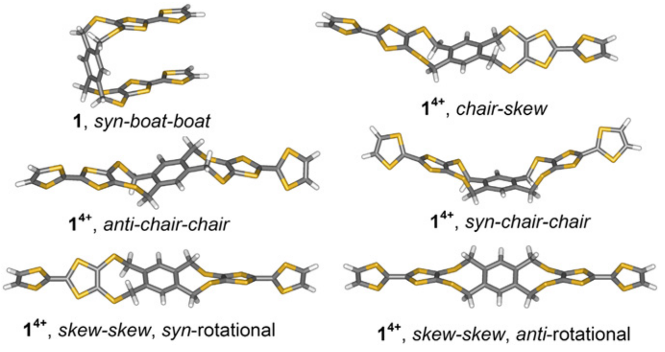


Figure 5. (a) Variable-temperature ^1H NMR spectra of tweezer **1a** (CD_2Cl_2, 2 mM) showing the transition from the dynamically flexible structure (293 K) to the tightly *closed* conformation (193 K); (b) low-temperature COSY spectrum of **1a** (193 K, 360 MHz, CD_2Cl_2).


1, *syn-boat-boat*

$\mathbf{1}^{4+}$, *chair-skew*

$\mathbf{1}^{4+}$, *anti-chair-chair*

$\mathbf{1}^{4+}$, *syn-chair-chair*

$\mathbf{1}^{4+}$, *skew-skew, syn*-rotational

$\mathbf{1}^{4+}$, *skew-skew, anti*-rotational

Figure 6. Comparison between *closed* conformation of **1** and several stable *open* conformations of $\mathbf{1}^{4+}$ (R, R^1=H). Geometry minimization was performed using PM3 method.

not show significant energy preference for any of the conformations of **1**, for $\mathbf{1}^{4+}$ only the conformations with large distance between charged TTF moieties (>15 Å) would be energetically stable (Fig. 6): *chair–chair* (both *syn*- and *anti*-), *skew–skew* (both *syn*- and *anti*-rotational), and *chair–skew* all lying within 2.5 kcal/mol (AM1) or 4 kcal/mol (PM3) energy range (Table 2). Other conformations, which have one or both of the eight-membered rings in the *boat* conformation and thus relatively short TTF–TTF distances, were driven to one of the stable conformations during geometry optimization. Electrostatic repulsion is the stabilizing force for the *open* conformations of $\mathbf{1}^{4+}$ as it is clearly seen (Table 2) from the energy difference between *anti*- and *syn-chair–chair* conformations: a reduction of ca. 0.7 Å in the distance between the charged TTF moieties costs about 2.5 kcal/mol in energy. Thus, several low-lying conformations for the tetracation $\mathbf{1}^{4+}$ were theoretically predicted. Interconversion between them, that can proceed through relatively low-barrier transition states, proceeds fast on the NMR timescale at 193 K and higher temperatures and leads to averaging of H^c and H^f protons.

The preferential conformation of the dication $\mathbf{1}^{2+}$ in solution can only be speculated about. Although initially it was claimed that cation radicals of TTF exist mostly in dimerized form $(TTF^{+\bullet})_2$ forming so called π-dimers,[25c] it was reported later[24a] that dimerization of tetrathioalkyl radical cations could not be detected in solution. Dimerization of non-substituted $TTF^{+\bullet}$ radical cations was observed at low temperatures by ESR[24a] as well as in solid state by X-ray crystallography,[16b,c] displaying fairly short average interplanar distances of 3.32–3.38 Å. Spatial preorganization of TTF groups in **1** is likely to facilitate their stacking even in solution, where electrostatic repulsion between the charged moieties cannot be compensated by the adjacent counter ions. Future ESR measurements are likely to clarify conformational preferences of the oxidized states.

Table 2
Relative energies and average TTF–TTF distances[a] of the low-energy conformations of $\mathbf{1}^{4+}$ (R, R^1=H)

	PM3		AM1	
	Energy, kcal/mol	Distance,[a] Å	Energy, kcal/mol	Distance, Å
anti-Chair–chair	0	16.01	0	15.70
syn-Chair–chair	2.52	15.22	2.45	15.07
Chair–skew	2.36	16.05	0.54	15.74
syn-Skew–skew	3.65	16.43	0.17	16.05
anti-Skew–skew	3.75	16.43	0.23	16.04

[a] Distance measured between the centers of the inner double bonds of TTF moieties.

Another open question is how energetically strong can the stroke of the opening motion be if we consider the opening motion from the *closed* to one of the *open* conformations upon oxidation to tetracation. Rough estimations using the PM3 method showed that the energy of the stroke arises to ca. 70 kcal/mol, if the minimized *closed* conformation of **1** is considered as a starting point—an energy amount almost equal to the average strength of a carbon–carbon bond. Such a significant energy output can make **1a** a valuable switching building block for the construction of functional dynamic molecular architectures.

3. Conclusions

In conclusion, we have presented new molecular tweezers containing two TTF units and capable of reversible large-scale switching between two profoundly different conformations upon oxidation/reduction. The new functional molecular architecture is a perspective scaffold for the construction of electrochemically responsive molecular machines and, after proper modification, also of tweezers-type molecular receptors. The preorganization of TTF moieties in these systems gives a unique opportunity to investigate the TTF–TTF dimerization process in solution and estimate the TTF–TTF pairing energy. The system also opens an opportunity for further studies of TTF–TTF interactions in the mixed-valence dimers $[(TTF)_2]^{+\bullet}$ and cation dimers (π-dimers) $([TTF]^{+\bullet})_2$ using spectroelectrochemical and ESR methods.

4. Experimental section

4.1. General

Reagent grade chemicals and solvents were used without further purification unless otherwise stated. All reactions were carried out under Ar or N_2 atmosphere. ^1H and ^{13}C NMR spectra were recorded with Bruker Avance DPX-200 and Bruker Avance WB-360 spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane using the residual solvent peak as internal reference: $CDCl_3$ (7.26 ppm for ^1H, 77.23 ppm for ^{13}C), CD_2Cl_2 (5.32 ppm for ^1H). Variable-temperature NMR (VT-NMR) measurements were performed on Bruker Avance WB-360 using internal temperature reference. ESI-MS spectra were measured on Bruker Esquire LC spectrometer using direct injection method and MALDI spectra were measured on PerSeptive Biosystems Voyager DE Pro spectrometer with 2,5-dihydroxybenzoic acid used as a matrix. UV/vis spectra were recorded with Varian Cary 50 Conc spectrophotometer; oxidative titrations of TTF derivatives were performed in stabilizer-free degassed dichloromethane by the addition of 0.01 or 0.02 M $NOSbF_6$ solution in acetonitrile. Melting points (mp) were obtained with an electrothermal capillary melting-point apparatus and were not corrected. Thin layer chromatography (TLC) was performed on silica gel aluminum cards from Fluka with F-254 fluorescent indicator. Flash chromatography (FC) was carried out using silica gel 60 from Fluka 230–440 mesh (particle size 36–70 μm).

4.2. Synthetic procedures

4.2.1. Synthesis of compounds **1**, general procedure

TTF derivative **3** (0.4 mmol) was dissolved in dry DMF (8 mL) and degassed by a freeze–pump–thaw cycle; then CsOH (0.84 mmol, 1.68 mL) was added as 0.5 M solution in MeOH at 0 °C. The mixture was allowed to warm to room temperature and stirred for 30 min, turning from orange to dark brown-red in color. Compound **4** (0.2 mmol) was dissolved in dry THF (4 mL), the solution was degassed by a freeze–pump–thaw cycle. Both solutions were simultaneously added in 3–4 equal portions to a degassed DMF/THF 2:1 mixture (15 mL) with intervals of 10 min while vigorously stirring. The reaction mixture turned orange-yellow, sometimes a precipitate formed. The mixture was allowed to stir for additional 30 min, and then was evaporated to dryness, the residue was redissolved in CH_2Cl_2, and the solution was washed with water and brine, dried (Na_2SO_4), and evaporated. The residue was purified by flash chromatography on silica gel.

4.2.2. Compound **1a**

Chromatography (CH_2Cl_2/PE 3:1) afforded an orange-red product in 56% yield. Mp: 102–104 °C. R_f=0.38 (SiO_2; CH_2Cl_2/PE 2:3). ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ 0.87 (12H, t, J=6.6 Hz, H^g), 0.96 (6H, t, J=7.0 Hz, H^k), 1.22–1.65 (44H, m), 1.88 (4H, quint., J=7.2 Hz, H^i), 2.74 (8H, t, J=7.0 Hz, H^f), 4.13 (4H, t, J=6.8 Hz, H^h), 4.32 (8H, s, H^c). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ 14.23, 14.37, 22.73, 22.90, 25.85, 28.43, 29.87, 30.43, 31.52, 31.97, 32.22, 36.51, 77.42 (C^c), 109.20, 115.66, 127.63 (C^e), 129.50 (C^d), 130.32 (C^b), 152.19 (C^a). UV/vis (CD_2Cl_2): λ_{max} (ε) 307 (31,300), 331 (28,800), 410 (sh., 3800) nm. HRMS (MALDI, DHB): calcd for $C_{58}H_{86}O_2S_{16}$ [M^+] 1326.2157, found 1326.2097. NMR assignment was performed on the basis of HMBC spectrum (see Supplementary data, Fig. S2).

4.2.3. Compound **1b**

Chromatography (CH_2Cl_2) afforded an orange-red product in 41% yield. Mp: 220–223 °C (decomp.). R_f=0.71 (SiO_2; CH_2Cl_2/PE 2:1). ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ 0.87 (12H, t, J=6.8 Hz), 1.24–1.65 (32H, m), 2.75 (8H, t, J=7.0 Hz), 4.27 (8H, s), 7.07 (2H, s). ^{13}C NMR (90 MHz, $CDCl_3$, 25 °C): δ 14.20, 22.77, 28.45, 29.92, 31.54, 36.60, 38.10, 127.79, 129.77, 132.91, 135.25. UV/vis (CD_2Cl_2): λ_{max} (ε) 297 (29,900), 336 (30,300), 410 (sh., 4800) nm. HRMS (MALDI, DHB): calcd for $C_{46}H_{62}S_{16}$ [M^+] 1126.0384, found 1126.0488.

4.2.4. Compound **1c**

Chromatography (CH_2Cl_2/PE 3:1) afforded a dark yellow product in 42% yield. Mp: 236–239 °C (decomp.). R_f=0.2 (SiO_2; CH_2Cl_2/PE 1:1). ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ 0.96 (6H, t, J=7.0 Hz), 1.32–1.62 (12H, m), 1.89 (4H, quint., J=7.2 Hz), 2.35 (12H, s), 4.16 (4H, t, J=6.8 Hz), 4.32 (8H, s). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ 14.40, 19.29, 22.93, 25.89, 30.46, 32.01, 77.43, 110.03, 115.43, 127.32, 129.23, 130.26, 152.28. UV/vis (CD_2Cl_2): λ_{max} (ε) 305 (29,100), 328 (25,000), 410 (sh., 3900) nm. HRMS (MALDI, DHB): calcd for $C_{38}H_{46}O_2S_{16}$ [M^+] 1045.9028, found 1045.8758.

4.2.5. 2,3,6,7-Tetrakis(hexylthio)tetrathiafulvalene **5**[25g]

Orange-red crystalline solid. Mp: 26–28 °C. ^{1}H NMR (200 MHz, CD_2Cl_2, 25 °C): δ 0.89 (12H, t, J=6.6 Hz), 1.22–1.47 (24H, m), 1.63 (8H, quint., J=7.4 Hz), 2.82 (8H, t, J=7.4 Hz). UV/vis (CD_2Cl_2): λ_{max} (ε) 311 (15,600), 332 (15,700) nm.

4.2.6. Oxidation of TTF derivatives, general procedure

A solution of the corresponding TTF derivative (1–2 mM) in CD_2Cl_2 was degassed by a freeze–pump–thaw cycle, cooled to −40 °C, and a 0.1 M solution of $NOSbF_6$ in CD_3CN (2 equiv for each TTF unit) was added dropwise. After 30 min the solution was degassed one more time to remove traces of NO and sealed in an NMR tube.

4.2.7. Compound $\mathbf{1^{4+}\cdot 4SbF_6^-}$

Deep blue in CD_2Cl_2 solution. ^{1}H NMR (360 MHz, CD_2Cl_2, 25 °C): δ 0.90 (12H, t, J=7.0 Hz, H^g), 0.97 (6H, t, J=7.2 Hz, H^k), 1.32–1.61 (36H, m), 1.87–1.96 (12H, m), 3.45 (8H, t, J=7.2 Hz, H^f), 3.89 (4H, t, J=6.4 Hz, H^h), 4.74 (8H, s, H^c). UV/vis (CD_2Cl_2): λ_{max} (ε) 307 (24,000), 728 (49,000) nm.

4.2.8. 2,3,6,7-Tetrakis(hexylthio)tetrathiafulvalene, bis-hexafluoroantimonate $\mathbf{5^{2+}\cdot 2SbF_6^-}$

Deep blue in CD_2Cl_2 solution. ^{1}H NMR (200 MHz, CD_2Cl_2, 25 °C): δ 0.90 (12H, t, J=6.8 Hz), 1.26–1.58 (24H, m), 1.90 (8H, quint., J=7.4 Hz), 3.42 (8H, t, J=7.0 Hz). UV/vis (CD_2Cl_2): λ_{max} (ε) 748 (22,000) nm.

4.3. Cyclic voltammetry

Experiments were performed with a computer controlled Autolab potentiostat in a three-electrode single-compartment cell (5 mL). The platinum working electrode consisted of a platinum wire sealed in a soft glass tube with a surface of A= 0.785 mm^2, which was polished down to 0.5 μm with Buehler polishing paste prior to use in order to obtain reproducible surfaces. The counter electrode consisted of a platinum wire and the reference electrode was an Ag/AgCl secondary electrode. For the measurements, concentrations of 5×10^{-3} mol L^{-1} of the electroactive species were used in freshly distilled and deaerated dichloromethane (Lichrosolv, Merck) and 0.1 M tetrabutylammonium hexafluorophosphate (Bu_4NPF_6, Fluka), which was twice recrystallized from ethanol and dried under vacuum prior to use.

4.4. Determination of activation energies

To estimate the free energy of activation at the temperature of coalescence Eq. 1 was used to treat a coalescing equally populated degenerate two-site uncoupled system and Eq. 2 was used for a coalescing AB system with an exchange between A and B protons:[27]

$$\Delta G_c^{\ddagger} = aT[9.972 + \log(T/\delta\nu)] \tag{1}$$

$$\Delta G_c^{\ddagger} = aT\left[9.972 + \log\left(T/\left(\delta\nu^2 + 6J_{AB}^2\right)^{1/2}\right)\right] \tag{2}$$

T is the temperature in Kelvin, $\delta\nu$ [Hz] the chemical shift between two coalescing resonances in the absence of exchange, J is a coupling constant for AB system, and a=4.575×10^{-3} for $\Delta G_c^{\ddagger}$ in kcal/mol. Coalescing H^f broadened multiplets (for assignment see Fig. 5a) were treated as broadened singlets using Eq. 1, whereas for coalescing AB system of H^c Eq. 2 was used. Activation energies obtained using H^f and H^c laid within 0.3 kcal/mol.

4.5. Molecular modeling

Molecular modeling was performed using HyperChem Release 7.0 for Windows (HyperCube, Inc.). Conformational searches were done using MM+ force field using analogues with O-substituted eight-membered rings due to inadequate parametrization for sulfur atoms in the force field. Geometry of low-lying conformations was further optimized after the substitution of O-atoms with S-atoms using semi-empirical AM1 and PM3 (RHF) methods.

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Supplementary data

Supplementary data (^{1}H and ^{13}C NMR and ESI-MS of the new compounds, ^{1}H NMR of $\mathbf{1a^{4+}\cdot 4SbF_6^-}$ and $\mathbf{5^{2+}\cdot 2SbF_6^-}$ as well as VT-NMR of $\mathbf{1a^{4+}\cdot 4SbF_6^-}$) associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.11.110.

References and notes

1. For reviews on molecular machines, see: (a) Kay, E. R.; Leigh, D. A.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 72–191; (b) *Acc. Chem. Res.* **2001**, *34*, 410–522 (Special issue on molecular machines); (c) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348–3391; (d) *Molecular Switches*; Feringa, B. L., Ed.; Wiley-VCH: Weinheim, Germany, 2001; (e) Balzani, V.; Venturi, M.; Credi, A. *Molecular Devices and Machines: A Journey into the Nano World*; Wiley-VCH: Weinheim, Germany, 2003.
2. (a) Kelly, T. R.; Silva, R. A.; De Silva, H.; Jasmin, S.; Zhao, Y. *J. Am. Chem. Soc.* **2000**, *122*, 6935–6949; (b) Koumura, N.; Zijlstra, R. W. J.; van Delden, R. A.; Harada, N.; Feringa, B. L. *Nature* **1999**, *401*,

152–155; (c) ter Wiel, M. K. J.; van Delden, R. A.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc.* **2003**, *125*, 15076–15086; (d) Fujita, T.; Kuwahara, S.; Harada, N. *Eur. J. Org. Chem.* **2005**, 4533–4543.

3. (a) Jiménez, M. C.; Dietrich-Buchecker, C.; Sauvage, J.-P. *Angew. Chem., Int. Ed.* **2000**, *39*, 3284–3287; (b) Jiménez-Molero, M. C.; Dietrich-Buchecker, C.; Sauvage, J.-P. *Chem. Commun.* **2003**, 1613–1616; (c) Jeppesen, J. O.; Nielsen, K. A.; Perkins, J.; Vignon, S. A.; Di Fabio, A.; Ballardini, R.; Gandolfi, M. T.; Venturi, M.; Balzani, V.; Becher, J.; Stoddart, J. F. *Chem.—Eur. J.* **2003**, *9*, 2982–3007; (d) Jeppesen, J. O.; Nygaard, S.; Vignon, S. A.; Stoddart, J. F. *Eur. J. Org. Chem.* **2005**, 196–220; (e) Nygaard, S.; Leung, K. C.-F.; Aprahamian, I.; Ikeda, T.; Saha, S.; Laursen, B. W.; Kim, S.-Y.; Hansen, S. W.; Stein, P. C.; Flood, A. H.; Stoddart, J. F.; Jeppesen, J. O. *J. Am. Chem. Soc.* **2007**, *129*, 960–970; (f) Balzani, V.; Clemente-León, M.; Credi, A.; Ferrer, B.; Venturi, M.; Flood, A. H.; Stoddart, J. F. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 1178–1183; (g) Badjic, J. D.; Ronconi, C. M.; Flood, A. H.; Stoddart, J. F.; Balzani, V.; Silvi, S.; Credi, A. *J. Am. Chem. Soc.* **2006**, *128*, 1489–1499; (h) Bottari, G.; Leigh, D. A.; Pérez, E. M. *J. Am. Chem. Soc.* **2003**, *125*, 13360–13361.
4. (a) Amabilino, D. B.; Dietrich-Buchecker, C. O.; Livoreil, A.; Pérez-García, L.; Sauvage, J.-P.; Stoddart, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 3905–3913; (b) Asakawa, M.; Ashton, P. R.; Balzani, V.; Credi, A.; Hamers, C.; Mattersteig, G.; Montalti, M.; Shipway, A. N.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Venturi, M.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 333–337; (c) Korybut-Daszkiewicz, B.; Więckowska, A.; Bilewicz, R.; Domagała, S.; Woźniak, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1668–1672; (d) Deng, W.-Q.; Flood, A. H.; Stoddart, J. F.; Goddard, W. A., III. *J. Am. Chem. Soc.* **2005**, *127*, 15994–15995.
5. (a) Berl, V.; Huc, I.; Khoury, R. G.; Krische, M. J.; Lehn, J.-M. *Nature* **2000**, *407*, 720–723; (b) Barboiu, M.; Lehn, J.-M. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5201–5206; (c) Dolain, C.; Maurizot, V.; Huc, I. *Angew. Chem., Int. Ed.* **2003**, *42*, 2738–2740.
6. (a) Chen, C.-W.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 4921–4922; (b) Zimmerman, S. C.; VanZyl, C. M. *J. Am. Chem. Soc.* **1987**, *109*, 7894–7896; (c) Rowan, A. E.; Elemans, J. A. A. W.; Nolte, R. J. M. *Acc. Chem. Res.* **1999**, *32*, 995–1006; (d) Klärner, F.-G.; Kahlert, B. *Acc. Chem. Res.* **2003**, *36*, 919–932; (e) Harmata, M. *Acc. Chem. Res.* **2004**, *37*, 862–873; (f) Petitjean, A.; Khoury, R. G.; Kyritsakas, N.; Lehn, J.-M. *J. Am. Chem. Soc.* **2004**, *126*, 6637–6647; (g) Colquhoun, H. M.; Zhu, Z. *Angew. Chem., Int. Ed.* **2004**, *43*, 5040–5045; (h) Pardo, C.; Sesmilo, E.; Gutiérrez-Puebla, E.; Monge, A.; Elguero, J.; Fruchier, A. *J. Org. Chem.* **2001**, *66*, 1607–1611.
7. (a) Kurebayashi, H.; Sakaguchi, M.; Okajima, T.; Haino, T.; Usui, S.; Fukazawa, Y. *Tetrahedron Lett.* **1999**, *40*, 5545–5548; (b) Kurebayashi, H.; Haino, T.; Fukazawa, Y. *Tetrahedron Lett.* **2000**, *41*, 477–480; (c) Kurebayashi, H.; Haino, T.; Usui, S.; Fukazawa, Y. *Tetrahedron* **2001**, *57*, 8667–8674; (d) Iwamoto, H.; Yamaguchi, M.; Hiura, S.; Fukazawa, Y. *Heterocycles* **2004**, *63*, 2005–2011; (e) Iwamoto, H.; Takahashi, N.; Maeda, T.; Hidaka, Y.; Fukazawa, Y. *Tetrahedron Lett.* **2005**, *46*, 6839–6842.
8. (a) Azov, V. A.; Schlegel, A.; Diederich, F. *Angew. Chem., Int. Ed.* **2005**, *44*, 4635–4638; (b) Azov, V. A.; Schlegel, A.; Diederich, F. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1926–1940.
9. For reviews on TTF chemistry and applications, see: (a) Bendikov, M.; Wudl, F.; Perepichka, D. F. *Chem. Rev.* **2004**, *104*, 4891–4945; (b) Segura, J. L.; Martín, N. *Angew. Chem., Int. Ed.* **2001**, *40*, 1372–1409; (c) Nielsen, M. B.; Lomholt, C.; Becher, J. *Chem. Soc. Rev.* **2000**, *29*, 153–164; (d) Bryce, M. R. *J. Mater. Chem.* **2000**, *10*, 589–598; (e) Becher, J.; Jeppesen, J. O.; Nielsen, K. *Synth. Met.* **2003**, *133–134*, 309–315.
10. (a) Gómez, R.; Segura, J. L.; Martín, N. *Org. Lett.* **2000**, *2*, 1585–1587; (b) Gómez, R.; Segura, J. L.; Martín, N. *J. Org. Chem.* **2000**, *65*, 7566–7574; (c) Zhou, Y.; Zhang, D.; Zhu, L.; Shuai, Z.; Zhu, D. *J. Org. Chem.* **2006**, *71*, 2123–2130; (d) Delogu, G.; Fabbri, D.; Dettori, M. A.; Sallé, M.; Le Derf, F.; Blesa, M.-J.; Allain, M. *J. Org. Chem.* **2006**, *71*, 9096–9103.
11. (a) Devonport, W.; Bryce, M. R.; Marshallsay, G. J.; Moore, A. J.; Goldenberg, L. M. *J. Mater. Chem.* **1998**, *8*, 1361–1372; (b) Bryce, M. R.; Devonport, W.; Goldberg, L. M.; Wang, C. *Chem. Commun.* **1998**, 945–951; (c) González, A.; Segura, J. L.; Martín, N. *Tetrahedron Lett.* **2000**, *41*, 3083–3086.
12. Jeppesen, J. O.; Nielsen, M. B.; Becher, J. *Chem. Rev.* **2004**, *104*, 5115–5131.
13. (a) González, M.; Segura, J. L.; Seoane, C.; Martín, N.; Garín, J.; Orduna, J.; Alcalá, R.; Villacampa, B.; Hernández, V.; López Navarrete, J. T. *J. Org. Chem.* **2001**, *66*, 8872–8882; (b) Bryce, M. R.; Martin, R.; Green, A.; Moore, A.; Perepichka, D. F.; Batsanov, A. S.; Howard, J. A. K.; Ledoux-Rak, I.; González, M.; Martín, N.; Segura, J. L.; Garín, J.; Orduna, J.; Alcalá, R.; Villacampa, B. *Eur. J. Org. Chem.* **2001**, *10*, 1927–1935; (c) Segura, J. L.; Priego, E. M.; Martín, N.; Luo, C.; Guldi, D. M. *Org. Lett.* **2000**, *2*, 4021–4024; (d) Gautier, N.; Dumur, F.; Lloveras, V.; Vidal-Gancedo, J.; Veciana, J.; Rovira, C.; Hudhomme, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 2765–2768; (e) Mas-Torrent, M.; Hadley, P.; Bromley, S. T.; Ribas, X.; Tarrés, J.; Mas, M.; Molins, E.; Veciana, J.; Rovira, C. *J. Am. Chem. Soc.* **2004**, *126*, 8546–8553.
14. (a) Pease, A. R.; Jeppesen, J. O.; Stoddart, J. F.; Luo, Y.; Collier, C. P.; Heath, J. R. *Acc. Chem. Res.* **2001**, *34*, 433–444; (b) Moonen, N. N. P.; Flood, A. H.; Fernandez, J. M.; Stoddart, J. F. *Top. Curr. Chem.* **2005**, *262*, 99–132.
15. (a) Chiang, P.-T.; Cheng, P.-N.; Lin, C.-F.; Liu, Y.-H.; Lai, C.-C.; Peng, S.-M.; Chiu, S.-H. *Chem.—Eur. J.* **2006**, *12*, 865–876; (b) Cheng, K.-W.; Lai, C.-C.; Chianga, P.-T.; Chiu, S.-H. *Chem. Commun.* **2006**, 2854–2856; (c) A very recent report describes flexible TTF-containing molecular tweezers: Poulsen, T.; Nielsen, K. A.; Bond, A. D.; Jeppesen, J. O. *Org. Lett.* **2007**, *9*, 5485–5488.
16. (a) Tachikawa, T.; Izuoka, A.; Sugawara, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1227–1229; (b) Tachikawa, T.; Izuoka, A.; Sugawara, T. *Solid State Commun.* **1993**, *88*, 207–209; (c) Fujiwara, H.; Arai, E.; Kobayashi, H. *J. Mater. Chem.* **1998**, *8*, 829–831.
17. (a) Kurebayashi, H.; Mine, T.; Harada, K.; Usui, S.; Okajima, T.; Fukazawa, Y. *Tetrahedron* **1998**, *54*, 13495–13504; (b) Anet, F. A. L.; Kozerski, L. *J. Am. Chem. Soc.* **1973**, *95*, 3407–3408; (c) Montecalvo, D.; St.-Jacques, M.; Wasylishen, R. *J. Am. Chem. Soc.* **1973**, *95*, 2023–2024; (d) Dunitz, J. D.; Waser, J. *J. Am. Chem. Soc.* **1972**, *94*, 5645–5650.
18. (a) Sinnokrot, M. O.; Valeev, E. F.; Sherrill, C. D. *J. Am. Chem. Soc.* **2002**, *124*, 10887–10893; (b) Sinnokrot, M. O.; Sherrill, C. D. *J. Phys. Chem. A* **2006**, *110*, 10656–10668.
19. (a) Simonsen, K. B.; Svenstrup, N.; Lau, J.; Simonsen, O.; Mørk, P.; Kristensen, G. J.; Becher, J. *Synthesis* **1996**, 407–418; (b) Svenstrup, N.; Rasmussen, K. M.; Hansen, T. K.; Becher, J. *Synthesis* **1994**, 809–812.
20. Compound **4a**, R^1=OC_6H_{13}: (a) Röhrich, J.; Wolf, P.; Enkelmann, V.; Müllen, K. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1377–1379; (b) Röhrich, J.; Müllen, K. *J. Org. Chem.* **1992**, *57*, 2374–2379.
21. Compound **4b**, R^1=H: Ried, W.; Bodem, H. *Chem. Ber.* **1956**, *89*, 2328–2331.
22. González, M.; Illescas, B.; Martín, N.; Segura, J. L.; Seoane, C.; Hanack, M. *Tetrahedron* **1998**, *54*, 2853–2866.
23. Moses, P. R.; Chambers, J. Q. *J. Am. Chem. Soc.* **1974**, *96*, 945–946.
24. (a) Khodorkovsky, V.; Shapiro, L.; Krief, P.; Shames, A.; Mabon, G.; Gourgues, A.; Giffard, M. *Chem. Commun.* **2001**, 2736–2737; (b) Giffard, M.; Mabon, G.; Leclair, E.; Mercier, N.; Allain, M.; Gorgues, A.; Molinié, P.; Neilands, O.; Krief, P.; Khodorkovsky, V. *J. Am. Chem. Soc.* **2001**, *123*, 3852–3853; (c) Kreicberga, Y. N.; Neilands, O. Y. *Zh. Org. Khim.* **1985**, *21*, 2009–2010.
25. (a) Jørgensen, M.; Lerstrup, K. A.; Bechgaard, K. *J. Org. Chem.* **1991**, *56*, 5684–5688; (b) Blanchard, P.; Svenstrup, N.; Becher, J. *Chem. Commun.* **1996**, 615–616; (c) Spanggaard, H.; Prehn, J.; Nielsen, M. B.; Levillain, E.; Allain, M.; Becher, J. *J. Am. Chem. Soc.* **2000**, *122*, 9486–9494; (d) Le Derf, F.; Levillain, E.; Trippé, G.; Gorgues, A.; Sallé, M.; Sebastian, R.-M.; Caminade, A.-M.; Majoral, J.-P. *Angew. Chem., Int. Ed.* **2001**, *40*, 224–227; (e) Bouguessa, S.; Hervé, K.; Golhen, S.; Ouahab, L.; Fabre, J.-M. *New J. Chem.* **2003**, *27*, 560–564; (f) Lyskawa, J.; Sallé, M.; Balandier, J.-Y.; Le Derf, F.; Levillain, E.; Allain, M.; Viel, P.; Palacin, S. *Chem. Commun.* **2006**, 2233–2235; (g) Frei, M.; Diederich,

F.; Tremont, R.; Rodríguez, T.; Echegoyen, L. *Helv. Chim. Acta* **2006**, *89*, 2040–2057.

26. The splitting of the second oxidation wave has been also observed for TTF-containing cyclophanes only when the TTF moieties were forced to stay in close proximity to each other. see: (a) Takimiya, K.; Imamura, K.; Shibata, Y.; Aso, Y.; Ogura, F.; Otsubo, T. *J. Org. Chem.* **1997**, *62*, 5567–5574; (b) Nielsen, M. B.; Thorup, N.; Becher, J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1305–1308.
27. Sandström, J. *Dynamic NMR Spectroscopy*; Academic: London, 1982; pp 93–123.