Expanding Tetra[2,3-thienylene]-Based Molecular Muscles to Larger [4*n*]Annulenes

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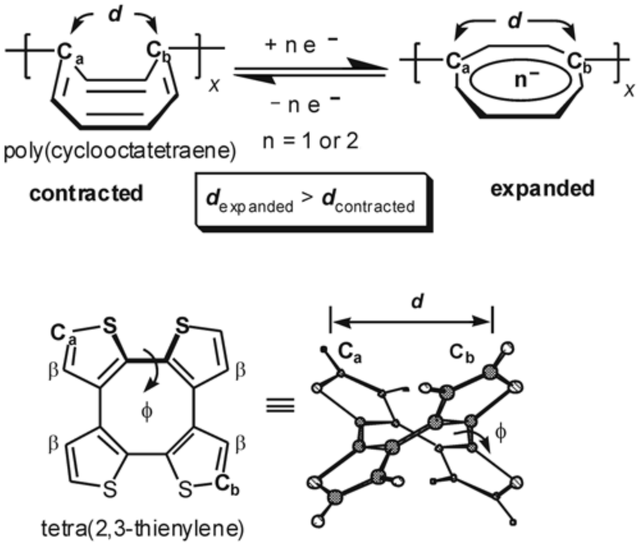
Received 1 March 2002

Abstract: The synthesis, X-ray structure, and predicted redox-induced conformational dynamics of a thiophene-fused [12]annulene is reported. Regiospecific halogenation of the thiophene ring system and transition-metal catalyzed cross-couplings are key elements in the synthetic strategy. It is predicted (B3LYP/6-31G*) that redox-induced conformational changes yield significant dimensional changes in this annulene, thus establishing it as a candidate for single molecule actuation.

Key words: annulenes, thiophene, cross-coupling, actuators, macrocycles

Redox-active polymers are capable of functioning as bulk electromechanical actuators.[1] By definition, such materials are capable of converting *electrical energy* (redox chemistry; as opposed to *chemical energy*[2]) into a bulk dimensional change that can be harnessed to perform work.[3] In 1999 we reported the concept of a single molecule electromechanical actuator (a so-called *molecular muscle*).[4] As exemplified by the hypothetical poly(cyclooctatetraene) shown in Scheme 1, our design was based on harnessing the perturbation in distance, *d*, that occurs during a redox-induced tub-to-planar conformational change in an [8]annulene.[5] In an effort to integrate the conformational dynamics of an [8]annulene with the favorable electrochemical properties of polythiophene,[6] we utilized Kauffmann's thiophene fused [8]annulene, tetra[2,3-thienylene],[7,8] as our building block. Although theoretical calculations[9] predict poly(tetra[2,3-thienylene)] to function as planned (change in *d* as a function of oxidation state), the range of actuation (a function of accessible conformers) is limited due to steric interactions between peripheral β-thienyl hydrogens (Scheme 1). Herein we report the synthesis, X-ray structure, and anticipated conformational dynamics of an *expanded* tetra(2,3-thienylene), compound **1**. Theoretical calculations predict that relieving steric congestion by expanding from an [8]annulene to a [12]annulene core affords a molecular actuator exhibiting a range of actuation more than double that of tetra(2,3-thienylene)-based materials.

As stated, planarization of tetra(2,3-thienylene) is severely inhibited by the spatial orientation of peripheral β-thienyl hydrogen atoms. This fact is reflected by the relatively high barrier for ring inversion, a value determined to be ca. 24 kcal/mol. Calculations at the PM3 level of theory predict the planar conformer of tetra(2,3-thienylene) is inaccessible over all oxidation states from 2^- to 2^+. For comparative purposes, note that the barrier to ring inversion for the *less* sterically congested [8]annulene, isopropylcyclooctatetraene, is ca. 14.8 kcal/mol,[10] while the *more* sterically congested [8]annulene, tetra-*o*-phenylene, is greater than 45 kcal/mol.[11] If complete planarity (ϕ = 0) were possible in tetra(2,3-thienylene), the range of actuation (d_{Ca-Cb}) would be 20%. However, steric crowding reduces this range to a predicted 6.7%.



Scheme 1

Compound **1** overcomes steric interactions between peripheral β-substituents by insertion of two alkyne spacers, thus rendering the 'expanded' tetrathienylene as a thiophene-fused didehydro[12]annulene. Given that a 4*n* -electron count is maintained within an elongated octagonal framework, a non-planar to planar redox-induced conformation change analogous to cyclooctatetraene is anticipated. Compound **1** is a regioisomer of the A-fragment of the octaaryl double helix, compound **2** (Figure 1), a system previously reported by us.[12] The similarity between isomers allows access via a similar synthetic strategy. As shown in Scheme 2, regiospecific bromination of commercially available 2-methylthiophene with NBS is followed by nickel catalyzed homocoupling to yield bithiophene **4**. Bromination of compound **4** is also regiospecific, and yields compound **5** in 72% yield. Lithi-

Synthesis 2002, No. 9, 01 07 2002. Article Identifier:
1437-210X,E;2002,0,09,1133,1135,ftx,en;C10902SS.pdf.

ISSN 0039-7881

um–iodine exchange converts **5** to the common building block in this synthesis, compound **6**. Diethynyl **7** is prepared via standard Pd/Cu(I) catalyzed cross coupling[13] of **6** with trimethylsilylacetylene (TMSA), followed by deprotection of the TMS group (compound **8**). Lastly, product **1** is obtained in 23% isolated yield via Pd/Cu(I) catalyzed cross-coupling of compounds **6** and **8**.

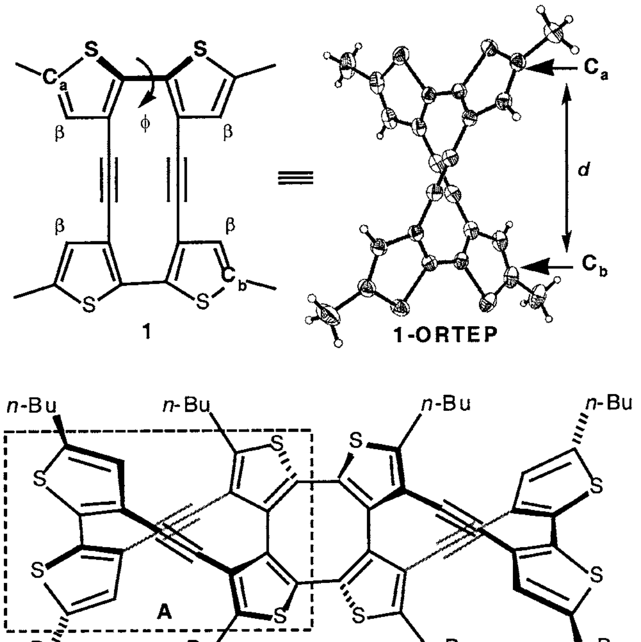
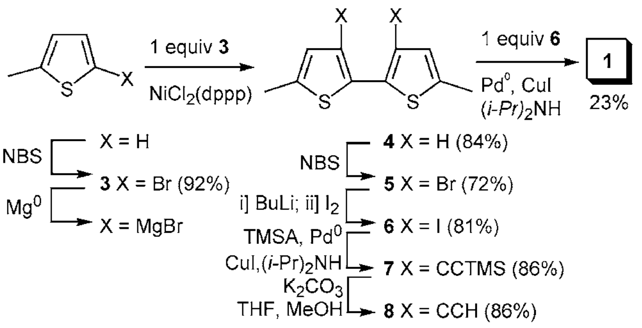


Figure 1 Showing compounds **1** and **2**.

The X-ray crystal structure of compound **1** is shown in Figure 1, and the twisted conformation is apparent.[14] The molecule adopts C_1 symmetry, with two unique S–C–C–S dihedral angles (ϕ) corresponding to 34.9 and 41.2. The average distance, *d*, is equal to 8.105Å. Density Functional Theory (B3LYP/6-31G*) was used to model the ground state geometry of compound **1**, less the four methyl sidechains. Figure 2 shows a comparison between bond lengths and dihedral angles as determined by experiment (average bond lengths) and theory. The agreement is relatively good given different symmetries (C_1 for X-ray and D_2 for theory), a difference that can be ascribed to packing forces in the crystal. Having established confidence with this level of theory, we probed the redox-induced conformational changes, both ϕ and *d*, by modeling the 2^-, 1^-, 1^+, and 2^+ oxidation states (all possess D_2 symmetry). The results are shown in Figure 2.

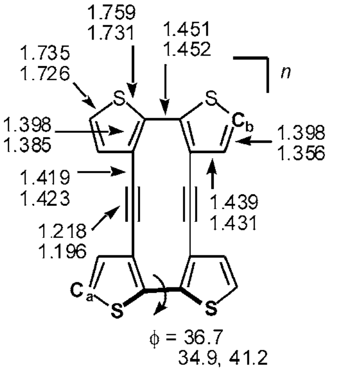
As can be seen from the predicted dihedral angles, a large redox-induced conformational change from twisted (ϕ = 36.7) to planar (ϕ = 0.0) occurs upon two-electron oxidation from a $4n$ to a $4n + 2$ -electron count. The corresponding change in distance, *d*, is 18%. Note that this range is more than double that predicted for tetra(2,3-thienylene) itself, a difference credited, in part, to a reduction in intramolecular sterics between adjacent β-thienyl positions. In further support, the barrier to inversion is calculated to be 9.7 kcal/mol, a value 14.3 kcal/mol lower in energy than the parent tetra(2,3-thienylene). Interestingly, each oxidation state of compound **1** is associated with a unique value of ϕ and *d*, thus yielding a range of actuation that may be attenuated across five unique oxidation states.



Scheme 2

In summary, the first two steps toward improved single molecule electromechanical actuators based on thiopene-fused [4*n*]annulenes have proven successful. First, the synthesis of an expanded tetra(2,3-thienylene), compound **1**, has been developed. Second, DFT calculations predict compound **1** to exhibit a large range in redox-induced conformational perturbations. Specifically, an 18% dimensional change is predicted for 1^{2+}. This large range of actuation is attributed, in part, to a reduction in the steric congestion resulting from β-substituent interactions in the parent tetra(2,3-thienylene) system. The next steps in this study will focus on the electrochemical properties of compound **1**, as well as its incorporation into a regiospecific homopolymer capable of translating the aforementioned *intrinsic* property of molecular electromechanical actuation throughout a single polymer chain.

All air and moisture-sensitive reactions were carried out in oven-dried glassware using standard Schlenk techniques under an inert atmosphere of dry nitrogen. Anhydrous solvents were dried over ac-



n	ϕ (deg)	$\Delta d_{Ca\text{-}Cb}$ (%)
2-	3.5	19
1-	15.9	16
0	36.7	-
1+	19.7	12
2+	0.0	18

Figure 2 Bond lengths and dihedral angle, ϕ. For bond lengths, the top entry corresponds to the calculated value (B3LYP/6-31G*; D_2 symmetry), and the bottom entry corresponds to the average of experimentally determined values (X-ray; C_1 symmetry), except in the case of ϕ (both unique values from X-ray data are provided). All bond lengths are reported in Å, and all dihedral angles are reported in degrees.

tivated alumina. Reagents were used as received from Acros, Aldrich, and Lancaster. Compounds **3**– **8** were prepared according to the literature methods reported for the synthesis of compound **2**. ^{1}H and ^{13}C NMR spectra were recorded with a Varian Inova-300 (300 MHz) spectrometer in $CDCl_3$. UV/Vis spectra were recorded on a Varian Cary 50Bio UV-Visible spectrophotometer. Mass spectra and high-resolution mass spectra were performed at the Southern California Regional Mass Spectrometry Facility (University of California at Riverside). Data for **1**-ORTEP: Crystal data: size 0.35 × 0.33 × 0.26 mm-^{3}, triclinic cell, a = 7.8365(8) Å, b = 12.5954(12) Å, c = 14.0004(13) Å, α = 63.300(2)^o, β = 84.201(2)^o, γ = 74.922(2)^o, V = 1191.8(2) Å^3, Z = 2, space group P-1. A sphere of reflections was collected (Bruker SMART1000 CCD detector, Mo X-ray). SHELXTL (Version 5.1) software was used for phase determination and structure refinement. Atomic coordinates, isotropic and anisotropic displacement parameters of all the non-hydrogen atoms were refined by means of a full matrix least-squares procedure on F^2.

2-Bromo-5-methylthiophene (3)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.86 (d, 1 H, *J* = 3.6 Hz), 6.54 (m, 1 H), 2.45 (d, 3 H, *J* = 1.2 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 141.54, 129.78, 125.69, 108.77, 15.32.

HRMS: Calcd for C_5H_5SBr: 175.9295. Found: 175.9289.

5,5′-Dimethyl-2,2′-bithiophene (4)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.90 (d, 2 H, *J* = 3.3 Hz), 6.48 (m, 2 H), 2.48 (s, 6 H). HRMS: Calcd for $C_{10}H_{10}S_2$: 194.0224. Found:194.0230.

3,3′-Dibromo-5,5′-dimethyl-2,2′-bithiophene (5)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.74 (d, 2 H, *J* = 1.2 Hz), 2.49 (d, 6 H, *J* = 1.2 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 141.88, 128.93, 126.89, 111.50, 15.71.

HRMS: Calcd for $C_{10}H_8S_2Br_2$: 349.8434. Found: 349.8434.

3,3′-Diiodo-5,5′-dimethyl-2,2′-bithiophene (6)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.82 (d, 2 H, *J* = 1.2 Hz), 2.50 (d, 6 H, *J* = 1.2 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 143.84, 133.68, 131.71, 84.51, 15.56.

HRMS: Calcd for $C_{10}H_8S_2I_2$: 445.8157. Found: 445.8159.

UV/Vis (THF): λ_{max} = 257 nm.

3,3′-Bis(trimethylsilylethynyl)-5,5′-dimethyl-2,2′-bithiophene (7)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.71 (d, 2 H, *J* = 1.2 Hz), 2.42 (d, 6 H, *J* = 1.2 Hz), 0.28 (s, 18 H).

HRMS: Calcd for $C_{20}H_{26}S_2Si_2$: 386.1014. Found: 386.1136.

3,3′-Diethynyl-5,5′-dimethyl-2,2′-bithiophene (8)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.76 (d, 2 H, *J* = 0.9 Hz), 3.33 (s, 2 H), 2.45 (d, 2 H, *J* = 0.9 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.64, 131.69, 129.07, 118.00, 82.45, 79.94, 15.33. HRMS: Calcd for $C_{14}H_{10}S_2$: 242.0224. Found: 242.0219.

UV/Vis (THF): λ_{max} = 239, 282, 354 nm.

Compound 1

To a solution of CuI (0.330 g, 1.73 mmol), Ph_3P(0.744g, 2.84mmol) and tris(dibenzylideneacetone)dipalladium(0) (0.181 g, 1.01mmol) in diisopropylamine (120 mL) was added a solution of compound **8** (0.348 g, 0.748mmol) and **6** (0.189 g, 0.748 mmol) via syringe pump at 70 °C. The addition was done under an atmosphere of argon over 4.5 h. The reaction mixture was cooled and concentrated in vacuo. The brown residue was extracted into Et_2O, and washed first with aq HCl (5%; 3 × 100 mL) and then with brine (100 mL). The organic layer was dried ($MgSO_4$). The Et_2O was removed by rotary evaporation. The resulting crude product was purified by silica gel column chromatography (hexanes–CH_2Cl_2) to give **1**

Yield: 23%; pale yellow solid.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.69 (d, 4 H, *J* = 1.2 Hz), 2.44 (d, 12 H, *J* = 1.2 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 139.96, 137.73, 131.76, 119.70, 90.99, 15.47.

HRMS: Calcd for $C_{24}H_{16}S_4$: 432.0135. Found: 432.0136.

UV/Vis (THF): λ_{max} = 239, 298 nm.

Acknowledgement

This work was supported by the National Science Foundation (CHE-9974548) and DuPont (Young Professor Award to M.J.M.).

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